EPA MRID Number 48683001

Data Requirement:

EPA DP Barcode

401651

OECD Data Point

229

EPA MRID

48683001

EPA Guideline

890.1350, Fish Short-Term Reproduction Assay

Test material:

Cypermethrin

Purity: 95.2%

Common name

Chemical name: IUPAC: mixture of the stereoisomers (S)-a-cyano-3-phenoxybenzyl (1RS,3RS;1RS,3SR)-3-

(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate where the ratio of the

(S);(1RS,3RS) isomeric pair to the (S);(1RS,3SR) isomeric pair lies in the ratio range

45-55 to 55-45 respectively

CAS name: (S)-cyano(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-

dimethylcyclopropanecarboxylate.

CA\$ No.: 52315-07-8

Synonyms: FMC 30980

EPA PC Code: 109703

Primary Reviewer: Joan Gaidos

Signature:

Senior Scientist, Cambridge Environmental, Inc.

Date: 1/07/13

Secondary Reviewer: Teri S. Myers

Signature:

Program Manager, CDM Smith

Date: 2/25/13

Primary Reviewer: Elizabeth Donovan

Date: 6/17/13 عبر المراكة الم

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EPA/EFED/ERB6

Additional Reviewer(s): Justin Housenger, Biologist

Date: 12/19/13

EPA/EFED/ERB5

Digitally signed by JUSTIN HOUSENGER DN: c=US, o=U.S. Governm OU-USEPA, DU-SLIFF, C1-JUSTIN HOUSENGER, O-QUARTER-0000044455 Date: 2015.06.11 11:05:33

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Additional Reviewer(s): Amy Blankinship, Chemist

Date:

AMY. **BLANKINSHIP**

EPA/EFED/ERB6

Date Evaluation Completed: 6/6/15

CITATION: York, D.O. 2012. Cypermethrin - Fish Short-term Reproduction Assay with the Fathead Minnow (Pimephales promelas). Performed by Smithers Viscient, Wareham, Massachusetts, Laboratory Project No. 1781.6766. Submitted by Syngenta Ltd, Jealott's Hill International Research Centre, Bracknell, Berkshire RG42 6EY, United Kingdom; FMC Corporation, Philadelphia, Pennsylvania; United Phosphorus, Inc., King of Prussia, Pennsylvania. Completion date April 18, 2012.

Note: The US EPA Endocrine Disruptor Screening Program (EDSP) Tier 1 screening battery is comprised of eleven screening assays intended to identify a chemical's likely endocrine bioactivity, i.e., its potential to interact with the estrogen, androgen, or thyroid (E, A, or T) pathways. The robustness of the Tier 1 battery is based on the strengths of each individual assay to identify potential endocrine bioactivity with complementary endpoints within the assay, where available, and redundancy across the battery. Thus, the results of each individual assay should not be considered in isolation but rether should be considered in the context of other assays in the battery as well as Other Scientifically Relevant Information (OSRI). In order to determine if e chemical has the potential to interact with the E, A or T pathweys, a Weight of Evidence (WoE) evaluation of Tier 1 assay results, in combination with the findings in the OSRI, should be undertaken (refer to the WoE Document).

Guideline recommendations are provided in italics; these recommendations should remain visible in the completed DER.

Disclaimer: The guideline recommendations in this DER template are offered as a general reference to aid in preparation of the DER. The purpose of these recommendations is not to serve as substitute for the Test Guidelines, nor to provide any guidance on how the study sheuld be conducted.

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EXECUTIVE SUMMARY:

The 21-day short-term reproduction assay of cypermethrin with fathead minnows (*Pimephales promelas*) was conducted under flow-through conditions. Adult fish (16 spawning groups, 2 males and 4 females in each group; 5 months old) were exposed to cypermethrin (95.2% purity) at nominal concentrations of 0 (control), 0.000030, 0.00030, and 0.003 mg a.i./L; mean-measured concentrations were <LOQ (<0.000001), 0.000013, 0.00012, and 0.0014 mg a.i./L. The test system was maintained at 25 to 26°C and a pH of 7.0 to 7.7.

There were no significant differences in either male or female survival at any treatment levels compared to the negative control. Percent survival was 100% for all groups of males and was 100, 94, 94, and 88% for the negative control and low, mid, and high treatment concentrations, respectively, for females. During the in-life exposure, there were no notable observations that occurred with regards to behavior, coloration/banding, changes in ovipositor appearance, or size of the dorsal nape pad, and no clinical signs of toxicity were observed. There were no treatment-related effects on male and female body weight and length.

Spawning occurred at least every 4 days in thee of the four control replicates and mean fecundity in control averaged 14 eggs/female/day/replicate (range: 13-18 eggs/female/day among the replicates); fertilization success in the control group averaged 96%. Fecundity was decreased (p<0.05) by 42% and 84% in the midand high-treatment females, respectively. There were no treatment-related effects (p>0.05) on fertilization success.

Male gonadal somatic index (GSI) was increased (p<0.05) by 22 and 27% at the mid and high treatment concentrations, respectively, compared to the negative control. There were no treatment-related effects on female GSI (p>0.05) or male and female plasma vitellogenin (VTG). Additionally, there were no significant effects on median male tubercle score, and no tubercles were observed on any females.

Although not analyzed statistically, in male fish, there were only background or sporadic genedal histopathological findings noted that were not considered related to treatment. In female fish, there was an increased incidence of mature occyte atresia at the high treatment concentration, which was associated with

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granulomatous inflammation and the presence of microsporidia in half the observed cases across all treatment

levels. There were no significant findings observed in the gonadal stage for either males or females, and no

notable observations in secondary sex characteristics for any treatment group compared to the controls.

The performance criteria for fecundity was not met. There were one replicate in the control group (Replicate

C) where there was a period of 4 days in which no spawning occurred and fecundity was 13 eggs/female/day.

Therefore, this replicate did not meet the criteria of either at least 15 eggs/female/day or spawning at least

every 4 days. However, it is noted that the overall control mean fecundity value (14) was just slightly below

15 eggs/female/day, and the other two replicates did achieve 15 or greater eggs/female/day and the

remaining replicate spawned at least every 4 days (11 eggs/female/day). Also, the %CV values for the mean

recoveries at the two highest treatment concentrations were 45.6 and 51.2%, which did not meet the validity

criteria of <20% over the 21-day test. There was no pattern of decline during the study period and no un-

dissolved test substance was observed in the dilution system, as such, the recoveries indicate the test material

was generally poorly recovered in solution under the test conditions. Given the physicochemical properties of

cypermethrin, these results may be considered consistent with expectations for the chemical and previous

experience with the test item. The remaining validity criteria for OCSPP 890.1350 were met. Therefore, while

these deviations are noted, they did not sufficiently impact the interpretation of the assay results.

There was one fish that was inadvertently counted as a female but later discovered to be a male. This occurred

in one of the control replicates and data from that replicate were subsequently reanalyzed for the gender

specific endpoints of male GSI, male VTG, body weight, and length. This did not have an impact on the

conclusions of the study as male GSI remained the only male gender specific endpoint with significant effects.

This assay satisfies the EDSP Tier 1 Test Order requirements for a Fish Short-Term Reproduction Assay

(OCSPP Guideline 890.1350).

Results Syriopsis

Test Organism age at test initiation: ca. 5 months

Mean body weight at test initiation (if measured): Male 3.2 g; Female 1.7 g

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Mean length at test initiation (if measured): Not reported.

Test Type (Flow-through, Static, Static Renewal): Flow-through

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Table 1: Summary of Reproductive and HPG Effects^{1,2} in the Fish Short-Term Reproduction Assay (FSTRA) with Cypermethrin.

Treatment	Gert Sign		Tubercle	Score	G	SI	Gonad	al Histo.	Plasm	a VTG	Plasr	na T	Plasn	na E2
(mg a.i./L) [mean- measured]	Fecundity	Fert. Success	M	F	М	F	M	F	M	F	M	F	М	F
0.000013	No	No	No	NA	No	No	NA	NA	No	No	NA	NA	NA	NA
0.00012	Yes	No	No	NA	Yes	No	NA	NA	No	No	NA	NA	NA	NA
0.0014	Yes	No	No	NA	Yes	No	NA	NA	No	No	NA	NA	NA	NA

Abbreviations: Concentration. Diff. Difference. E2 17β-estradiol. Female. Fert. Fertilization. GSI Gonado-Somatic Index. Histopathology.

Male. NA Not applicable. T Testosterone. VTG Vitellogenin.

A "yes" indicates a significant difference based on comparison to the negative (clean water) control, unless otherwise specified.

The criteria for significance are described in the Reviewer's Analysis and Statistical Verification sections of the DER. Conclusions regarding histopathology may be heavily weighted by the expert opinion of a board-certified pathologist.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED:

This study was conducted according to the U.S. EPA OCSPP 890.1350: "Fish Short-Term Reproductive Assay" and OECD 229 (2009). The following deviations were noted:

- 1. There were one replicate in the control group (Replicate C) where there was a period of 4 days in which no spawning occurred, and fecundity was 13 eggs/female/day, respectively. Therefore, this replicate did not meet the criteria of either at least 15 eggs/female/day or spawning at least every 4 days. However, it is noted that the overall control mean fecundity value (14) was just slightly below 15 eggs/female/day, and the other two replicates did achieve 15 or greater eggs/female/day and the remaining replicate spawned at least every 4 days (11 eggs/female/day).
- 2. Analytical verification of the test material from Days 0, 6, 11, 19 and 21 yielded recoveries of 44% to 67% of nominal concentrations. Results of these analyses indicate measured concentrations where generally lower than nominal, but according to the study author were consistent with expectations for the physicochemical properties and previous experience with the test item. Therefore, although there was no pattern of decline during the study period and no undissolved test substance was observed in the dilution system, the recoveries indicate the test material was generally poorly recovered in solution under the test conditions. The %CV values for the mean recoveries at the two highest treatment concentrations were 45.6 and 51.2%, which did not meet the validity criteria of <20% over the 21-day test. The test material was detected on Days 11 (one replicate) and 19 (two replicates) in the control samples. The study author's concluded the contamination was likely a result of processing samples after being removed from the exposure system and that the control fish were not exposed to cypermethrin.</p>
- 3. The physico-chemical properties of the test material were not reported.

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- 4. The unionized ammonia and residual chlorine in the test water were not reported. The OCSPP 890.1350 performance criteria establish maximum levels for these values and it is unclear if the maximum recommendations were exceeded.
- Incorrect sexing of individuals in one replicate from the control group resulted in there being three males and three females in this replicate instead of the two males and four females specified in the OCSPP 890.1350 guideline.

These deviations do not sufficiently impact the acceptability of the study.

COMPLIANCE:

Signed and dated No Data Confidentiality, GLP, and Quality Assurance statements were provided. This study was conducted in compliance with all pertinent U.S. EPA Good Laboratory Practice regulations with the following exceptions: routine dilution water and food contaminant screening analyses were conducted following standard validated methods. This exception has no impact on the study results.

A. TEST MATERIAL:

Cypermethrin; CAS# 52315-07-8.

Description:

Amber liquid.

OECD recommends describing water solubility, melting/boiling point stability in water and light, pKa, Pow or Kow, vapor pressure of test compound, expiration date.

Lot No./Batch No.:

PL10-0492

Purity:

95.2%

Impurities:

None reported

Stability of Compound: Analytical verification of the test material from Days 0, 6, 11, 19 and 21 yielded recoveries of 44% to 67% of nominal concentrations. Stock solution (FETAX) fortified with cypermethrin at concentrations of 0.000003, 0.00005, and 0.0005 mg a.i./L yielded recoveries of 80.9 to 96.8% of nominal concentrations. Quality control samples (n=17) fortified at 0.000015, 0.0003, and 0.003 mg a.i./L yielded recoveries of 83.0 to 118% of nominal concentrations. Results of these analyses indicate measured concentrations where generally lower than nominal, but according to the study author were consistent with expectations for the physicochemical properties and previous experience with the test item. Therefore, although there was no pattern of decline during the study period and no un-dissolved test substance was observed in the dilution system, the recoveries indicate the test material was generally poorly recovered in solution under the test conditions. Additionally, the %CV values were 45.6 and 51.2% for the 0.00012 and 0.0014 mg a.i./L treatment concentrations, respectively, and did not meet the validation criteria of <20%.

Storage Conditions of Test Chemicals: Stored at room temperature in a dark, ventilated cabinet.

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B. Test organism:

Table 2: General Information About the Test Species and Acclimation.

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Species common name:	Fathead Minnow		EPA recommends fathead minnow
Species scientific name:	Pimephales promelas		(Pimephales promelas).
Species strain (if stated):	Not reported		
Were fish obtained from a single laboratory stock?	Yes		EPA recommends that fish be from a single laboratory stock.
Were acclimation conditions same as definitive test?	Yes		EPA recommends that fish be acclimated under water quality and illumination conditions that are similar to the definitive test.
Acclimation period:	16 days		EPA recommends a minimum two-week acclimation period. Note that the acclimation period is different from the subsequent, in situ pre-exposure phase.

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Details on health:		No mortalities were reported during the 7 days prior to pre-exposure period.	EPA recommends that mortality during the 7 days prior to the pre-exposure phase be less than 5% of the culture population. If
		Fish did not receive any treatment for disease in the two weeks prior to spawning (pre-exposure period).	mortality during these 7 days is greater than 10%, EPA recommends that the fish be rejected. If mortality is between 5-10%,
		Behavioral abnormalities or clinical signs were not reported.	EPA recommends that fish be held another 7 days. If mortalities greater than 5% occur during this extended acclimation period,

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Type of food: Source of food:	Frozen brine shrimp Not reported	Representative samples of the food source were periodically analyzed for pesticides, PCBs, and toxic metals by GeoLabs, Inc. and analyte levels were below LOC specified by ASTM (2005).	EPA recommends that fish be fed frozen brine shrimp twice per day to promote active reproduction and maintain body condition.
Frequency of feeding:	2 times/day		
Details on feeding:	None.		

Table 3: Fish Selection and Pre-Exposure Performance.

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Age at test initiation:	Ca. 5 months	Ca. 20 weeks old	EPA recommends reproductively mature (sexually dimorphic) fish, 4.5 - 6 months old.

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Mean weight of males at test initiation (if determined):	3.2 g	Based on 20 males used to stock aquaria for pre-exposure phase.	EPA recommends that a subsample of fish be weighed before the test to estimate the
Range of individual weights (males) at test initiation (if determined):	2.8 to 3.7	Individual weights within ±20% of the estimated mean.	mean weight for each sex. It is recommended that the individual weight of each fish selected for the test be within ±20% of the estimated mean for each sex.
Mean weight of females at test initiation (if determined):	1.7 g	Based on 20 females used to stock aquaria for pre-exposure phase.	120% of the estimated mean for each sex.
Range of individual weights (females) at test initiation (if determined):	1.3 10 2.0	Individual weights within ±20% of the estimated mean.	
Mean length of males at test initiation (if determined):	Not reported		
Mean length of females at test initiation (if determined):	Not reported		
Duration of pre-exposure phase:	16 days		EPA recommends a minimum of 14 days.

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Were pre-exposure conditions identical to the definitive test?	Yes		EPA recommends that pre-exposure conditions, including temperature, photoperiod, feeding, etc., be identical to definitive test conditions.
Number of pre-exposure tanks:	36	Extra replicates were established to account for a potential lack of spawning in some chambers and/or mortality during this phase.	EPA recommends that additional tanks set up at the beginning of pre-exposure will ensure that sufficient replicates with the correct sex ratio are available for the definitive test.
Number of males per tank:	2		
Number of females per tank:	4		•
Pre-exposure fecundity:	≥15 eggs/female/ reproductive day/ replicate		EPA recommends that pre-exposure fecundity in each replicate (tank) selected for use in the definitive test be at least 15 eggs/female/reproductive day/replicate during the 7 days prior to the definitive test

Parameter · ·	Value(s)	Details or Remarks	Guideline Recommendations
Number of spawns during pre- exposure:	≥two times in 7 days		EPA recommends that spawning occur at least twice in the 7 days prior to the definitive test.
Details on pre-exposure:		None.	

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C. Exposure System

Table 4: Summary of Information on the Exposure System and Test Vessel Characteristics.

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Type of exposure:	Flow-through		EPA recommends the use of a flow- through system. As noted in the Corrections and Clarifications document', the use of a static renewal system is not recommended for this assay.
Type of flow-through dilution system:	Intermittent flow proportional diluters		Intermittent flow proportional diluters or continuous flow serial diluters are recommended. ²

U.S. Environmental Protection Agency (EPA). (2011). Corrections and Clarifications on Technical Aspects of the Test Guidelines for the Endocrine Disruptor Screening Program Tier 1 Assays (OCSPP Test Guideline Series 890). March 3, 2011. Office of Chemical Safety and Pollution Prevention (OCSPP), Washington, D.C. (http://www.epa.gov/endo/pubs/assayvalidation/clarificationdoc.pdf).

Additional guidance for aquatic test design is located in OCSPP Guideline 850.1000, Special Considerations for Conducting Aquatic Laboratory Studies.

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Flow-through rate:	Ca. 45 mL/minute or 2.7 L/hr and 6.6 volume replacements/day.	Calculated by the reviewer based on 0.5 L/cycle, 131 cycles/24 hrs and 60 minutes/hr.	Recommended flow-through rate is 45 mL/min (2.7 L/hr), or at least 6 total volume exchanges per day.
Details on toxicant mixing for flow-through systems:		Flow-splitting chambers were used between diluter cells and the 4 replicate test vessels. Treatment recoveries were not measured	Recommended toxicant mixing for flow- through systems: 1) Mixing chamber is recommended but not required; 2) Aeration is not recommended for mixing; 3) A demonstration that the test solution
		prior to test initiation to indicate if diluter had reached equilibrium. Flow splitting accuracy not reported.	is completely mixed before introduced into the test system is recommended; 4) The recommended flow splitting accuracy is within 10%.
Aeration?	None reported.		EPA recommends aeration if dissolved oxygen reaches <4.9 mg/L (< 60% saturation).

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Source of dilution water:	Well water		EPA recommends natural or reconstituted water; it is recommended that natural water be sterilized with UV and tested for pesticides, heavy metals, and other possible contaminants. OECD accepts any water in which the test species show control survival at least as good as indicated in the test guideline.
Was dilution water analyzed for pesticides, heavy metals, and other contaminants?	Yes		
Test vessel type/materials:	Glass aquaria with silicone adhesive.		EPA and OECD recommend that water- contact portions of the system not compromise the study (e.g., all glass vessels or glass vessels with stainless steel frames are acceptable examples).

Parameter .	Value(s)	Details or Remarks	Guideline Recommendations
Test vessel size:	20 cm wide x 39 cm long x 25 cm high		EPA recommends the use of 18 L test chambers (e.g., 40 x 20 x 20 cm).
Fill volume:	10 L		EPA recommends 10 L solution per tank
Spawning substrate material: Spawning substrate size:	4 inch diameter aged PVC cut lengthwise in half (arches) and into 7 cm sections. Aged PVC cut in half		EPA recommends that each tank contains three semi-circular spawning substrates, e.g., aged PVC pipe, 10 - 20 cm in length, split lengthwise.
	(arches) and into 7 cm sections.		
Additional details on exposure system:		None.	

Table 5: Summary of Water Quality Characteristics in the Test System.

Parameter	Minimum	Maximum	Mean	Measurement Interval	Guideline Recommendations
Temperature (°C)	25	26	25.5	Continuously	EPA recommends temperature 25±f°C; inter-replicate and inter-treatment differentials should not exceed f°C.
рН	7.0	7.7	7.35	Weekly	EPA recommends pH 6.5 to 9.0.
Dissolved oxygen (mg/L)	4.9 (61%)	8.2 (98%)	6.6 (79.5%)	Weekly	EPA recommends dissolved oxygen (DO) ≥4.9 mg/L (>60% air saturation)
Total alkalinity (mg/L as CaCO ₃)	20	26	23	Weekly	EPA recommends total alkalinity >20 mg/L as CaCO ₃ .
Hardness (mg/L as CaCO ₃)	48	60	54	Weekly	
Total organic carbon (mg/L)	0.30	0.42	0.36	Twice	EPA recommends that total organic carbon in dilution water be ≤2 mg/L.
Unionized ammonia (μg/L)	Not reported	Not reported	Not reported	Not reported	EPA recommends that unionized ammonia in the dilution water be ≤1 μg/L.

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Parameter	Minimum	Maximum	Mean	Measurement Interval	Guideline Recommendations
Residual chlorine (μg/L)	Not reported	Not reported	Not reported	Not reported	EPA recommends that residual chlorine in dilution water be <10 μg/L.
Conductivity (μmhos/cm)	260	340	300	Weekly	General recommendations for frequency of measurements: EPA recommends that temperature, pH, and dissolved oxygen be measured in all test tanks at least weekly and that hardness and alkalinity be measured in controls and in one tank at the highest test concentration at least weekly. In addition, continuous temperature monitoring of at least one tank is encouraged.

Abbreviations: NA Not applicable.

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D. Study Design and Additional Experimental Conditions

Table 6: Range-Finding Study Conditions (if Applicable).

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Was a range-finder conducted?	Yes		EPA recommends conducting a range-finder if 96-hour LC _{so} data for the fathead minnow are unavailable.
If yes, what was the method for determining the highest test concentration in the range-finder?	14 day LC _{so} value range finding study.	Nominal test concentrations of 0 (negative and acetone controls), 0.00063, 0.0013, 0.0025, 0.0050 and 0.010 mg/L.	EPA recommends that the highest test concentration be selected based on toxicity data for other fish studies or species, if available. Otherwise, either the solubility limit of the test compound or 100 mg/L (whichever is lower) is appropriate.
Species:	Pimephales promelas		
Life stage:	Not reported		EPA recommends that range-finding tests be performed with fish of similar age and size to those that would be utilized in the test.

Parameter .	Value(s)	Details or Remarks	Guideline Recommendations
Test duration:	14 day		EPA recommends a 96-hour exposure.
Additional details:	The test was conducted under flow-through conditions. On Days 12 and 13, two female fish at the highest treatment level were observed at solution's surface. At test termination, 40%		EPA recommends conducting a range-finder with five test concentrations plus a control (six total treatment levels), with four females and two males per exposure tank (36 fish total). The number of mortalities that occur may be used to develop a concentration-response curve. Based upon the results, the highest concentration that does not result in
	combined male and female mortality was observed at the highest level. No other mortalities or sub-lethal effects were observed.		increased mortality or signs of overt morbidity compared to controls, or 1/3 the derived 96-hr LC ₅₀ , may be selected as the highest exposure concentration in the 21-day test.

Table 7: Definitive Study Conditions.

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Test duration:	21 days		EPA recommends that the duration of the definitive test be 21 days.
Method for selecting the highest test concentration in the definitive test:	The toxicity 14 day LC _{so} value was estimated to be >0.010 mg/L.		EPA recommends that the highest test concentration is either the solubility limit of the test compound, 100 mg/L, or demonstrates adequate evidence of toxicity (e.g., 1/3 the 96-hour LC ₅₀), whichever concentration is lowest.
Reference study citation (if applicable):	NA		
Separation of test concentrations:	0 (control), 0.00003, 0.0003, and 0.003 mg a.i./L	Step down factor of 10 from highest test concentration.	EPA suggests that a concentration separation of between 0.33 (or three-fold) and 0.1 (or ten-fold) is scientifically acceptable.

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Number of test concentrations:	4		EPA recommends a minimum of 3 concentrations and a control, plus solvent control if appropriate.
Are nominal concentrations adjusted for purity?	Yes		
Indicate the type of values presented for measured concentrations:	Mean measured		
Limit of quantification (LOQ):	<0.000001 mg a.i./L		EPA recommends that for chemical test concentrations below the LOQ, analyses be conducted on the stock solutions.
Level of detection (LOD):	Not reported		

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Frequency of measurement:	O, 4, 6, 11, and 19 days		It is recommended that test item concentration be measured prior to the addition of fish in all tanks and at least weekly thereafter in two replicates per treatment level.
Was the randomized complete block design used?	Yes		EPA recommends that all fish be randomly assigned to tanks during pre-exposure. Tanks are then ranked according to pre-exposure fecundity, and the tanks with the highest fecundity are randomly assigned to a definitive test treatment and block first. Each block contains one replicate of each treatment, including controls.
Number of replicates in control:	4		EPA recommends 4 replicates.
Number of replicates in solvent control (if applicable):	NA		EPA recommends the use of a concurrent solvent control when a solubilizing agent is used. EPA recommends 4 replicates.

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Number of replicates per test item treatment level:	4		EPA recommends 4 replicates.
Number of male fish per replicate at test initiation:	2		EPA recommends 2 males per replicate.
Number of female fish per replicate at test initiation:	4		EPA recommends 4 females per replicate.
Was a solvent used?	No		
Solvent type (if applicable):	NA		
Maximum solvent concentration (if applicable):	NA		EPA recommends that the solvent not exceed 0.02 ml/L ³ . OECD recommends that solvent have no effect on survival nor produce any other adverse effects and that concentration not be greater than 0.1 ml/L ³

Hutchinson TH, Shillabeer N, Winter MJ, Pickford DB (2006). Acute and chronic effects of carrier solvents in aquatic organisms: A critical review. Review. Aquatic Toxicology, 76, pp.69-92.

OECD (2000), Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures. Environmental Health and Safety Publications. Series on

Parameter	Value(s)	Details or Remarks	Guideline Recommendations
Was a positive control used?	No		
Positive control (if applicable):	NA		
Positive control concentration(s)	NA		
(if applicable):			
Photoperiod:	16 hrs light:		EPA recommends photoperiod 16:8
	8 hrs dark		(light:dark).
Light intensity at water's	550-1000 lux	Fluorescent bulbs	EPA recommends light intensity 540 -
surface:			1080 lux (at water's surface).
Additional details:	None.		

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Table 8: Summary of Treatment Concentrations in the Fish Short-Term Reproduction Assay with Cypermethrin.

Treatment ID	Nominal Concentration (mg a.i./L)	Mean Measured Concentration ¹ (mg a.i./L)	Mean CV (%)	Details or Remarks	Guideline Recommendations
Control (dilution water only)	<0.000001	<loq< td=""><td colspan="3">EPA recommends that test item concentrations be maintained at a coefficient</td></loq<>	EPA recommends that test item concentrations be maintained at a coefficient		
Solvent control (if applicable)	NA	NA	NA		of variation (CV) ≤20%.
Treatment 1	0.00003	0.000013	14.2	± 0.0.0016	
Treatment 2	0.0003	0.00012	45.6	± 0.0546	
Treatment 3	0.003	0.0014	51.2	± 0.7096	
Diluter Stock	NA	NA	NA		

Abbreviations: CV Coefficient of variation.

The mean measured values obtained by the study author are presented in the table and were calculated using the actual analytical results and not the rounded values presented. These values are different than the mean measured values obtained by the reviewer of 0.0000142, 0.00012 and 0.0014 mg a.i./L. LOQ=0.000001 mg a.i./L.

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E. Observations

Biological Endpoints: Surviv

Survival, fecundity, fertilization success, and clinical signs were observed daily. At test termination (Day 21), secondary sex characterization (body color, pattern, body shape), body weight, length, tubercle score, gonadal staging and histopathology, and plasma vitellogenin were evaluated.

Were raw (individual) data provided? Yes

EPA recommends that observations of survival, fecundity, fertilization success, secondary sex characteristics, and other clinical signs occur at least daily. At test termination (Day 21), additional observations include body weight and length, nuptial tubercle score, gonadal staging and histopathology, plasma vitellogenin, and plasma sex steroids (testosterone and 17ß-estradiol, if measured). Gonado-somatic index (GSI) is calculated using a ratio of gonad weight to body weight (gonad weight to the nearest 0.1 mg / body weight in mg x 100) at test termination.

Clinical signs of overt toxicity may include (but are not limited to) hemorrhage, cessation of feeding, and other abnormal behavior.

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II. RESULTS AND DISCUSSION

A. Results

Mean male survival values were 100% at all test levels, and female survival values were 100, 94, 94, and 88% in the mean-measured 0 (control), 0.000013, 0.00012, and 0.0014 mg a.i./L treatment levels, respectively (Table 9). The mortality rate in the water control was 0%, therefore, the survival rate in the control group satisfied the minimum acceptable control value criteria of ≥90% according to the USEPA OCSPP 890.1350 guideline. During the in-life exposure, no notable observations occurred with regards to behavior, coloration/banding, changes in ovipositor appearance or size of dorsal nape pad.

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Table 9: Adult Fish Survival in Fathead Minnow (Pimephales promelas).

Treatment		Males		Females			
(mg a.i./L) [mean-measured]	N¹	# Surviving	% Survival	n	# Surviving	% Survival	
Control (<loq)< td=""><td>9</td><td>9</td><td>100</td><td>15</td><td>15</td><td>100</td></loq)<>	9	9	100	15	15	100	
0.000013	8	8	100	16	15	94	
0.00012	8	8	100	16	15	94	
0.0014	8	8	100	16	14	88	

Abbreviations: NA Not applicable.

LOQ=0.000001 mg a.i./L.

Mean male body weight values were 3.10, 3.57, 3.60, and 3.18 g and female body weight values were 1.45, 1.47, 1.26 and 1.28 g in the mean-measured 0 (control), 0.000013, 0.00012 and 0.0014 mg a.i./L treatment levels, respectively (Table 10). Mean male body length values were 62.2, 64.1, 64.3, and 62.7 mm and female body length values were 50.5, 49.5, 48.5 and 50.5 mm in the mean-measured 0 (control), 0.000013, 0.00012 and 0.0014 mg a.i./L treatment levels, respectively.

¹ Total number of fish at test initiation.

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Table 10: Size at Test Termination in Fathead Minnow (Pimephales promelas).

		Body Weight						Length					
Treatment (mg a.i./L)		Males			Females	1		Males			Females		
[mean-measured]	'n	Mean (g)	±SD	n	Mean ±SD n Mean ±SD	±SD	n	Mean (mm)	±SD				
Control (<loq)< td=""><td>4</td><td>3.10</td><td>0.39</td><td>4</td><td>1.45</td><td>0.50</td><td>4</td><td>62.2</td><td>2.44</td><td>4</td><td>50.5</td><td>2.99</td></loq)<>	4	3.10	0.39	4	1.45	0.50	4	62.2	2.44	4	50.5	2.99	
0.000013	4	3.57	1.04	4	1.47	0.33	4	64.1	4.76	4	49.5	2.52	
0.00012	4	3.60	1.24	4	1.26	0.24	4	64.3	5.89	4	48.5	2.98	
0.0014	4	3.18	1.24	4	1.28	0.36	4	62.7	3.66	4	50.5	2.99	

Abbreviations: NA Not applicable. ND Not determined. SD Standard deviation.

LOQ=0.000001 mg a.i./L.

Mean fecundity values were 14, 13, 8.3 and 2.2 eggs/female/day and fertilization success was 96, 97, 96 and 92% in the mean-measured 0 (control), 0.000013, 0.00012 and 0.0014 mg a.i./L treatment levels, respectively (Table 11). Replicate B of the control group inadvertently contained three male and three female fish due to a mis-sexed fish.

Table 11: Fecundity and Fertilization Success in Fathead Minnow (Pimephales promelas).

Treatment (mg a.i./L) [mean- measured]	Fecundity ¹	±SD	Fertilization Success (%)²	±SD	
Control (<loq)< td=""><td>14</td><td>2.99</td><td>96</td><td>4.36</td></loq)<>	14	2.99	96	4.36	
0.000013	13	3.00	97	0.5	
0.00012	8.3	4.73	96	1.73	
0.0014	2.2	0.88	92	6.65	

Abbreviations: NA Not applicable. ND Not determined.

Fecundity is calculated as the number of eggs per surviving female per reproductive day per replicate.

Fertilization success (%) is calculated as the number of embryos divided by the number of eggs, multiplied by 100 LOQ=0.000001 mg a.i./L.

Median male tubercle scores were 32.5, 37, 33 and 25 in the mean-measured 0 (control), 0.000013, 0.00012 and 0.0014 mg a.i./L treatment levels, respectively (Table 12). None of the surviving females were found to have tubercles.

Table 12: Nuptial Tubercle Score in Fathead Minnow (Pimephales promelas).

Treatment		Males	Females		
(mg a.i./L) [mean-measured]	n	Median Tubercle Score	п	Median Tubercle Score	
Control (<loq)< td=""><td>4</td><td>32.5</td><td>4</td><td>0</td></loq)<>	4	32.5	4	0	
0.000013	4	37	4	0	
0.00012	4	33	4	0	
0.0014	4	25	4	0	

Abbreviations: NA Not applicable. ND Not determined. SD Standard deviation.

LOQ=0.000001 mg a.i./L.

Median male GSI was 1.1, 1.2, 1.4 and 1.4% and mean female GSI was 12, 11, 11 and 14% in the mean-measured O (control), 0.000013, 0.00012 and 0.0014 mg a.i./L treatment levels, respectively (Table 13).

Table 13: Gonado-Somatic Index (GSI) in Fathead Minnow (Pimephales promelas).

Treatment	Males			Females		
(mg a.i./L) [mean-measured]	n	Median GSI ¹ (%)	±SD	n	Mean GSI ¹ (%)	±SD
Control (<loq)< td=""><td>4</td><td>1.1</td><td>0.25</td><td>4</td><td>12</td><td>4.3</td></loq)<>	4	1.1	0.25	4	12	4.3
0.000013	4	1.2	0.19	4	11	2.2
0.00012	4	1.4	0.07	4	11	2,4
0.0014	4	1.4	0.22	4	14	1.6

Abbreviations: NA Not applicable.

Gonado-somatic index (χ) is calculated as gonad weight (to the nearest 0.1 mg) / body weight (mg) x 100. LQQ=0.000001 mg a.i./L.

Median male gonadal stage was 2, 2, 2 and 3 and median female gonadal stage was 3, 3, 3 and 3 in the mean-measured 0 (control), 0.000013, 0.00012 and 0.0014 mg a.i./L treatment levels, respectively (Table 14).

Table 14: Gonadal Staging in Fathead Minnow (Pimephales promelas).

Treatment		Males	Females				
(mg a.i./L) [mean-measured]	, n	Median Stage	n	Median Stage ²			
Control (<loq)< td=""><td>4</td><td>2</td><td>4</td><td>3</td></loq)<>	4	2	4	3			
0.000013	4	2	4	3			
0.00012	4	2	4	3			
0.0014	4	3	4	3			

Abbreviations: Juvenile, NA Not applicable, ND Not determined. UTS Unable to stage.

In male fish, there were only background or sporadic findings noted and were not related to treatment (Tables 15-16). In female fish, there was an increased incidence of mature oocyte atresia at the 0.0014 mg a.i./L treatment, which was associated with granulomatous inflammation and the presence of microsporidia in half the observed cases across all treatment levels (Tables 17-18).

The guideline recommends the following gonadal staging scale for male fathead minnow: O=undeveloped, 1=early spermatogenic, 2=mid-spermatogenic, 3=late spermatogenic, 4=spent.

The guideline recommends the following gonadal staging scale for female fathead minnow: O=undeveloped, 1=early development, 2=mid-development, 3=late development, 4=late development/hydrated, 5=post-ovulatory.
LOQ=0.000001 mg a.i./L.

Table 15: Gonadal Histopathology in Male Fathead Minnow (Pimephales promelas).

					Diagno	stic Ob	servations1				
Treatment (mg a.i./L) [mean- measured]	Severity	Pro	ncreased oportion of ermatogonia	But a	Presence of Testis-Ova		ncreased Testicular generation	Mir	Duct neralization	Interstitial cell (Leydig) hypertrophy/hyp rplasia	
Miles		n	Incidence	n	Incidence	n	Incidence	n	Incidence	n	Incidence
Control	0	9	7	9	8	9	8	NA	NA	NA	NA
(<loq)< td=""><td>1</td><td>9</td><td>1</td><td>9</td><td>1</td><td>9</td><td>1</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td></loq)<>	1	9	1	9	1	9	1	NA	NA	NA	NA
	2	9	1	9	0	9	0	NA	NA	NA	NA
	3	9	0	9	0	9	0	NA	NA	NA	NA
	4	9	0	9	0	9	0	NA	NA	NA.	NA
0.000013	0	8	8	8	8	8	7	NA	NA	NA	NA
	1	8	0	8	0	8	0	NA	NA	NA	NA
	2	8	0	8	0	8	1	NA	NA	NA	NA
	3	8	0	8	0	8	0	NA	NA	NA	NA
	4	8	0	8	0	8	0	NA	NA	NA	NA
0.00012	0	8	6	8	8	8	8	NA	NA	NA	NA
	1	8	1	8	0	8	0	NA	NA	NA	NA
	2	8	1	8	0	8	0	NA	NA	NA	NA
	3	8	0	8	0	8	0	NA	NA	NA	NA
	4	8	0	8	0	8	0	NA	NA	NA	NA
0.0014	0	8	8	8	8	8	8	NA	NA	NA	NA
	1	8	0	8	0	8	0	NA	NA	NA	NA
	2	8	0	8	0	8	0	NA	NA	NA	NA
	3	8	0	8	0	8	0	NA	NA	NA	NA
	4	8	0	8	0	8	0	NA	NA	NA	NA

Gonadal histopathology diagnostic observations are graded 0 - 4 based on severity: 0=Not remarkable, 1=Minimal,

²⁼Mild, 3=Moderate, 4=Severe. See Appendix E of the test guideline for reference. LOQ=0.000001 mg a.i./L.

Table 16: Additional Gonadal Histopathology Observations in Male Fathead Minnow (Pimephales promelas).

		Additional Diagnostic Observations ¹													
Treatment (mg a.i./L) [mean-measured]	Severity	Pro	ecreased oportion of rmatogonia	Increased Vascular or Interstitial Proteinaceous Fluid		Asynchronous Gonad Development		Altered Proportions of Spermatocytes or Spermatids		Granulomatous Inflammation					
	0	n	Incidence	n	Incidence	n	Incidence	n	Incidence	n	Incidence				
Control (<loq)< td=""><td>0</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td></loq)<>	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
	1	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
	2	NA	NA	NA.	NA	NA	NA	NA	NA	NA	NA				
	3	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
	4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
0.000013	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
	1	NA	NA	NA	NA.	NA	NA	NA	NA	NA	NA				
	2	NA	NA	NA.	NA	NA	NA	NA	NA	NA	NA				
	3	NA	NA	NA.	NA	NA	NA	NA	NA	NA	NA				
	4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				

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	1000	Additional Diagnostic Observations ¹													
Treatment (mg a.i./L) [mean-measured]	Severity	Pro	ecreased oportion of rmatogonia	Increased Vascular or Interstitial Proteinaceous Fluid		Asynchronous Gonad Development		of S	ed Proportions permatocytes Spermatids	Granulomatous Inflammation					
	0	n	Incidence	n	Incidence	n	Incidence	n	Incidence	n	Incidence				
0.00012	0	NA	NA	NA	NA	NA	NA	NA	NA.	NA	NA				
	1	NA	NA	NA	NA	NA	NA.	NA	NA	NA	NA				
	2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
	3	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
	4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
0.0014	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
	1	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
	2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
	3	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				
	4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA				

Gonadal histopathology diagnostic observations are graded 0 - 4 based on severity: 0=Not remarkable, 1=Minimal, 2=Mild, 3=Moderate, 4=Severe. See Appendix E of the test guideline for reference.

LOQ=0.000001 mg a.i./L.

Table 17: Gonadal Histopathology in Female Fathead Minnow (Pimephales promelas).

			Add	ditional	Diagnostic Ob	servati	ons ¹			
Treatment (mg a.i./L) [mean- measured]	Severity	Incre	ased Oocyte Atresia	Hy	follicular Cell yperplasia/ ypertrophy		reased Yolk formation	Aggregates of macrophages, multifocal		
measarca _j		п	Incidence	n	Incidence	n	Incidence	n	Incidence	
Control	0	15	15	NA	NA	NA	NA	NA	NA	
(<loq)< td=""><td>1</td><td>15</td><td>0</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td></loq)<>	1	15	0	NA	NA	NA	NA	NA	NA	
	2	15	0	NA	NA	NA	NA	NA	NA	
	3	15	0	NA	NA	NA	NA	NA	NA	
	4	15	0	NA	NA	NA	NA	NA	NA	
0.000013	0	15	13	NA.	NA	NA	NA	NA	NA	
	1	15	2	NA	NA	NA	NA	NA.	NA	
	2	15	0	NA	NA	NA	NA	NA	NA	
	3	15	0	NA	NA	NA	NA	NA	NA	
	4	15	0	NA	NA	NA	NA	NA	NA	
0.00012	0	15	14	NA	NA	NA	NA	NA	NA	
	1	15	1	NA	NA	NA	NA	NA	NA	
	2	15	0	NA	NA	NA	NA	NA	NA	
	3	15	0	NA	NA	NA	NA	NA	NA	
	4	15	0	NA	NA	NA	NA	NA	NA	

	TENED!	Additional Diagnostic Observations ¹													
Treatment (mg a.i./L) [mean- measured]	Severity	Incre	ased Oocyte Atresia	Hy	follicular Cell perplasia/ pertrophy		reased Yolk formation	Aggregates of macrophages, multifocal							
		n	Incidence	'n	Incidence	n	Incidence	n	Incidence						
0.0014	0	14	7	NA	NA	NA	NA	NA	NA						
	1	14	1	NA	NA	NA	NA	NA.	NA						
	2	14	3	NA	NA	NA	NA	NA	NA						
	3	14	3	NA	NA	NA	NA	NA	NA						
	4	14	0	NA	NA	NA	NA	NA	NA						

Gonadal histopathology diagnostic observations are graded 0 - 4 based on severity: 0=Not remarkable, 1=Minimal,

LOQ=0.000001 mg a.i./L.

Table 18: Additional Gonadal Histopathology Observations in Female Fathead Minnow (*Pimephales promelas*).

Treatment	4 5 - NO	Additional Diagnostic Observations ¹													
(mg a.i./L) [mean-	Severity	Interstitial fibrosis		Egg Debris in Oviduct			nulomatous flammation	Decreased Post							
measured]		n	Incidence	n	Incidence	n	Incidence	n	Incidence						
Control	0	NA	NA	15	13	15	14	NA	NA						
(<loq)< td=""><td>1</td><td>NA</td><td>NA</td><td>15</td><td>1</td><td>15</td><td>1</td><td>NA</td><td>NA</td></loq)<>	1	NA	NA	15	1	15	1	NA	NA						
	2	NA	NA	15	1	15	0	NA	NA						
	3	NA	NA	15	0	15	0	NA	NA						
	4	NA	NA	15	0	15	0	NA	NA						

²⁼Mild, 3=Moderate, 4=Severe. See Appendix E of the test guideline for reference.

Treatment		31 -	P	ddition	al Diagnostic	Observa	tions ¹		H. T. L. L.	
(mg a.i./L) [mean-	Severity	Inters	stitial fibrosis	Egg Debris in Oviduct			anulomatous flammation	Decreased Pos Ovulatory Follici		
measured]		n	Incidence	n	Incidence	n	Incidence	n	Incidence	
0.000013	0	NA	NA	15	15	15	13	NA	NA	
	1	NA	NA	15	0	15	2	NA	NA	
	2	NA	NA	15	0	15	0	NA	NA	
	3	NA	NA	15	0	15	0	NA	NA	
	4	NA	NA	15	0	15	0	NA	NA	
0.00012	0	NA	NA	15	15	15	13	NA	NA	
	1	NA	NA	15	0	15	2	NA	NA	
	2	NA	NA	15	0	15	0	NA	NA	
	3	NA	NA	15	0	15	0	NA	NA	
	4	NA	NA	15	0	15	0	NA	NA	
0.0014	0	NA	NA	14	13	14	11	NA	NA	
	1	NA	NA	14	0	14	0	NA	NA	
	2	NA	NA	14	1	14	3	NA	NA	
	3	NA	NA	14	0	14	0	NA	NA	
	4	NA	NA	14	0	14	0	NA	NA	

Gonadal histopathology diagnostic observations are graded 0 = 4 based on severity: 0=Not remarkable, 1=Minimal, 2=Mild, 3=Moderate, 4=Severe. See Appendix E of the test guideline for reference.

LOQ=0.000001 mg a.i./L.

Mean male VTG was 41, 53, 39 and 35 and female VTG was 1.2x10⁶, 8.4x10⁵, 1.1x10⁶ and 1.1x10⁶ ng/mL in the mean-measured 0 (control), 0.000013, 0.00012 and 0.0014 mg a.i./L treatment levels, respectively (Table 19).

Table 19: Plasma Vitellogenin in Fathead Minnow (Pimephales promelas).

and the second second			Plasma Vite	ellogenin	(VTG)	1/1/2/1
Treatment (mg a.i./L)		Males		1	Females	
[mean-measured]	n	Mean (ng/mL plasma)	±SD	n	Mean (ng/mL plasma)	±SD
Control (<loq)< td=""><td>4</td><td>41</td><td>34</td><td>4</td><td>1.2 x 10⁶</td><td>2.553 x 10⁵</td></loq)<>	4	41	34	4	1.2 x 10 ⁶	2.553 x 10 ⁵
0.000013	4	53	72	4	8.4 x 10 ⁵	2.34 x 10 ⁵
0.00012	4	39	25	4	1.1 x 10 ⁶	3.64 x 10 ⁵
0.0014	4	35	29	4	1.1 x 10 ⁶	3.01 x 10 ⁵

Abbreviations: NA Not applicable. ND Not determined. SD Standard deviation. LOQ=0.000001 mg a.i./L.

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Mean plasma testosterone and plasma 17β-estradiol in male and females was not measured (Table 20).

Table 20: Plasma Sex Steroids in Fathead Minnow (Pimephales promelas). Not measured.

			Plasma Te	stosterone	(T)		Plasma 17β-estradiol (E2)							
Treatment		Males			Females	21		Males		Females				
(mg a.i./L) [mean-measured]	n	Mean (ng/mL plasma)	±SD	n	Mean (ng/mL plasma)	±SD	n	Mean (ng/mL plasma)	±SD	n	Mean (ng/mL plasma)	±SD		
Control (<loq)< td=""><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td></loq)<>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA		
0.000013	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA		
0.00012	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA		
0.0014	NA .	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA		

Abbreviations: NA Not applicable. Not determined. SD Standard deviation.

LOQ=0.000001 mg a.i./L.

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There were no notable observations with regards to behavior or changes in appearance (coloration/banding, presence of ovipositor and dorsal nape pad), including secondary sex characteristics in the control or treated groups (Table 21). Replicate B in the control group contained three males and three females due to mis-sexed fish.

Table 21: Secondary Sex Characteristics and Clinical Signs in Fathead Minnow (Pimephales promelas).

Treatment	Secondary Sex Characteristics and Clinical Signs												
(mg a.i./L)	Male			Females									
[mean-measured]	Туре	n	Incidence	Туре	n	Incidence							
Control (<loq)< td=""><td>None</td><td>9</td><td>0</td><td>None</td><td>15</td><td>0</td></loq)<>	None	9	0	None	15	0							
0.000013	None	8	0	None	15	0							
0.00012	None	8	0	None	15	0							
0.0014	None	8	0	None	14	0							

LOQ=0.000001 mg a.i./L.

B. Study Author's Analysis and Conclusions

The study author analyzed tubercle score, GSI, fertility, fecundity, and VTG. Data were gender specific and analyzed in comparison to the controls.

Descriptive statistics (mean, standard deviation, etc.) were determined for each endpoint. Significant effects were detected for p<0.05 with the exception of Shapiro-Wilk's and Bartlett's Tests, which were based on p<0.01 (CETIS, version 1.8.4, 2011). Survival, body weight and body length data were recoded but not statistically analyzed. Fecundity, fertility, male and female VTG, and female GSI were analyzed using ANOVA and a one-tailed Dunnett's Multiple Comparison test. Median male tubercle scores and median male GSI were analyzed by ANOVA and Jonckheere-Terpstra Step-Down test. Male and female length was recorded but statistical analysis was not reported. Prior to Dunnett's, data were analyzed by Shapiro-Wilk's test and Bartlett's to test for normality and homogeneity of variances, respectively. If normality and homogeneity tests passed (p>0.01), a parametric analysis was performed using the transformed data. If non-normality or unequal variance were indicated (p<0.01), a non-parametric analysis was performed on the ranks of the data. These methods appear to be consistent with the methods recommended in the guideline.

There were no differences in male or female survival at any treatment level based on visual inspection of the data (Table 9). There was no statistically significant difference in fertilization success at any treatment level compared to the control (p>0.05; Dunnett's). There was a statistically significant reduction in fecundity at the 0.00012 and 0.0014 mg a.i./L treatment levels compared to the control (p<0.05; Dunnett's). However, the mean fecundity in the control was 14 eggs/female/day; OCSPP guidance requires fecundity in the controls of at least 15 eggs/female/day. There was a significant decrease in median male GSI at the 0.00012 and 0.0014 mg a.i./L treatment levels compared to the control (p<0.05; Jonckheere-Terpstra Step-Down test; Table 13). There were no significent differences between treated groups and control for any other endpoint.

In male fish, there were only background or sporadic gonadal histopathology findings noted which were not related to treatment (Tables 15-16). In female fish, there was an increased incidence of

mature oocyte atresia at the 0.0014 mg a.i./L treatment, which was associated with granulomatous inflammation and the presence of microsporidia in half the observed cases across all treatment levels (Tables 17-18). There were no significant findings observed in the gonadal stage for either males or females.

C. Reviewer's Analysis and Conclusions

Statistical Methods: The reviewer analyzed survival (mortality) data based on visual observation. Male GSI and fecundity were consistent with a monotonic concentration-response; no other endpoints were associated with a monotonic response. All data ware tested for normality using Shapiro-Wilks test and for homogeneity of variance using Levene's test. Data which met the assumptions of normality and homogeneity of variance were then analyzed using the parametric Dunnett's test. Data which did not meet the parametric assumptions were analyzed using the non-parametric Mann-Whitney U test. Male GSI and fecundity exhibited monotonic trends and was analyzed using the non-parametric Jonckheere-Terpstra test, as recommended by the OCSPP 890.1350 guideline.

None of the surviving females were found to have tubercles. Unless otherwise indicated, effects were considered statistically significant at p<0.05. These analyses were conducted using SAS® (SAS Institute, Cary, NC; version 8.1). The data was subsequently re-run for the gender-specific endpoints (male GSI, male VTG, male length, male weight) when excluding the mis-sexed male fish in the control group with CETIS (Version 1.8.7.12). Both the study author and reviewer relied on the mean-measured concentrations to discuss effects in this study.

Conclusions:

There were no significant differences in either male or female survival at any treatment levels compared to the negative control based on visual observation (Table 9). Male GSI exhibited a significant (p<0.05) increase of 22 to 27% at the 0.00012 and 0.0014 mg a.i./L treatment levels compared to the negative control. Fecundity was significantly (p<0.05) reduced 42% and 84% of control at the 0.00012 and 0.0014 mg a.i./L treatment level. There were no other significant

effects on all other endpoints (female GSI, male and female plasma VTG, male and female weight and length and male and female nuptial tubercle score).

Although not analyzed statistically, in male fish, there were only background or sporadic findings noted and were not related to treatment. In female fish, there was an increased incidence of mature oocyte atresia at the 0.0014 mg a.i./L treatment, which was associated with granulomatous inflammation and the presence of microsporidia in half the observed cases across all treatment levels.

There were no significant findings observed in the gonadal stage for either males or females, and no notable observations in secondary sex characteristics or clinical signs for any treatment group compared to the controls. Sex steroids were not measured in this study.

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Table 22: Reproductive and HPG Endpoints^{1,2} for Male Fathead Minnow (*Pimephales promelas*) in the FSTRA with Cypermethrin.

Treatment (mg a.i./L)	Tubercle	Score			Gonadal Staging and Histo.	Plasma VTG		Plasma T		Plasma E2	
[mean-measured]	Median	р	% Diff.	р	Effect? (Yes/No)	% Diff.	Р	% Diff.	р	% Diff.	р
Control (<loq)< td=""><td>32.5</td><td>NA</td><td>0</td><td>NA</td><td>No</td><td>0</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td></loq)<>	32.5	NA	0	NA	No	0	NA	NA	NA	NA	NA
0.000013	37	0.914	10.41	0.231	No	59.4	0.859	NA	NA	NA	NA
0.00012	33	0.600	22.17	0.041	No	18.05	0.994	NA	NA	NA	NA
0.0014	25	0.071	26.70	0.018	No	5.26	1.00	NA.	NA	NA	NA
Statistical Test	Mann-W	/hitney	Jonckh	neere's	NA	Dunr	nett's	N/		NA	

Abbreviations: Concentration. Diff. Difference. E2 17β-estradiol. GSI Gonado-Somatic Index. Histopathology. NA Not applicable. Testosterone. VTG Vitellogenin. NA Not applicable.

LOQ=0.000001 mg a.i./L.

Unless otherwise indicated, effects and percent (%) differences are reported based on comparison to the negative (clean water) control. Conclusions regarding histopathology may be heavily weighted by the expert opinion of a board-certified pathologist.

Unless otherwise specified, effects are considered statistically significant at p<0.05.</p>

EPA MRID Number 48683001

Table 23: Reproductive and HPG Endpoints^{1,2} for Female Fathead Minnow (*Pimephales promelas*) in the FSTRA with Cypermethrin.

Treatment (mg a.i./L)	Fecundity		Fert. Success			Tubercle Score		SI	Gonadal Staging and Histo.	Plasm	a VTG	Plasma T		Plasma E2	
[mean- measured]	% Diff.	р	% Diff.	Р	Median	P	% Diff.	p	Effect? (Yes/No)	% Diff.	P	% Diff.	P	% Diff.	р
Control (<loq)< td=""><td>0</td><td>NA</td><td>0</td><td>NA</td><td>0</td><td>NA</td><td>o</td><td>NA</td><td>No</td><td>0</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td><td>NA</td></loq)<>	0	NA	0	NA	0	NA	o	NA	No	0	NA	NA	NA	NA	NA
0.000013	-5.26	0.328	1.30	0.9140	0	NA	-5.05	0.979	No	-28.30	0.302	NA	NA	NA	NA
0.00012	-41.93	0.032	0.00	>0.05	0	NA	-5.68	0.971	No	-5.32	0.981	NA	NA	NA	NA
0.0014	-84.39	<0.001	-4.40	0.659	0	NA	20.00	0.492	No	-10.64	0.879	NA	NA	NA	NA
Statistical Test	Jonckh	neere's	Dunne	ett's T3	NA		Dunr	nett's	NA	Dunr	nett's	N	A	N	Α

Abbreviations: Concentration. Difference. E2 17β-estrediol. Fertilization. GSI Gonado-Somatic Index. Histopathology.

NA Not applicable. T Testosterone. VTG Vitellogenin.

¹ Unless otherwise indicated, effects and percent (%) differences are reported based on comparison to the negative (clean water) control. Conclusions regarding histopathology may be heavily weighted by the expert opinion of a board-certified pathologist.

 $^{^2\,}$ Unless otherwise specified, effects are considered statistically significant at p<0.05. LOQ=0.000001 mg a.i./L.

Table 24; Growth Endpoints1.2 in the Fish Short-Term Reproduction Assay (FSTRA) with Cypermethrin.

Treatment	7	Body	Weight		Length					
(mg a.i./L)	Males		Females		Males		Females			
[mean-measured]	% Diff.	р	% Diff.	р	% Diff.	р	% Diff.	p		
Control (<loq)< td=""><td>0</td><td>NA</td><td>0</td><td>NA</td><td>0</td><td>NA</td><td>0</td><td>NA</td></loq)<>	0	NA	0	NA	0	NA	0	NA		
0.000013	15.22	0.497	5.83	0.808	2.97	0.651	-2.37	0.502		
0.00012	16.16	0.435	-9.03	0.552	3.32	0.577	-4.43	0.102		
0.0014	2.64	0.993	-9.29	0.531	0.75	0.989	-1.55	0.768		
Statistical Test	Dunnett's		Dunnett's		Dunnett's		Dunnett's			

Abbreviations: Difference. NA Not applicable.

LOQ=0.000001 mg a.i./L.

E. Study Deficiencies

There were deviations in the validity and performance criteria and a couple of minor deviations described in Section I. Materials and Methods of this DER regarding failure to report certain water characteristics and meet environmental criteria:

1. There were one replicate in the control group (Replicate C) where there was a period of 4 days in which no spawning occurred, and fecundity was 13 eggs/female/day, respectively. Therefore, this replicate did not meet the criteria of either at least 15 eggs/female/day or spawning at least every 4 days. However, it is noted that the overall control mean fecundity value (14) was just slightly below 15 eggs/female/day, and the

Unless otherwise indicated, percent (%) differences are reported based on comparison to the negative (clean water) control.

Unless otherwise specified, effects are considered statistically significant at p<0.05.</p>

other two replicates did achieve 15 or greater eggs/female/day and the remaining replicate spawned at least every 4 days (11 eggs/female/day).

- 2. Analytical verification of the test material from Days O, 6, 11, 19 and 21 yielded recoveries of 44% to 67% of nominal concentrations. Additionally, the %CV values were 14.2, 45.6 and 51.2%, respectively, and did not meet the validation criteria of <20%. Results of these analyses indicate measured concentrations were generally lower than nominal, but according to the study author were consistent with expectations for the physicochemical properties and previous experience with the test item. Therefore, although there was no pattern of decline during the study period and no un-dissolved test substance was observed in the dilution system, the recoveries indicate the test material was generally poorly recovered in solution under the test conditions.</p>
- 3. The test material was detected at Days 11 (one replicate) and 19 (two replicates) in the control samples. The study author concluded that the contamination was not consistent among replicates and not consistent throughout exposure. The study author concluded the contamination was likely a result of processing samples after being removed from the exposure system, indicating the control fish were not exposed to cypermethrin.
- 4. The unionized ammonia and residual chlorine in the test water were not reported. The OCSPP 890.1350 performance criteria establish maximum levels for these values and it is unclear if the maximum recommendations were exceeded.
- Incorrect sexing of individuals in one replicate from the control group resulted in there being three males and three females in this replicate instead of the two males and four females specified in the OCSPP 890.1350 guideline.

These deviations did not sufficiently adversely impact interpretation of the assay results. The remaining validity and performance criteria for OCSPP 890.1350 were met.

F. Reviewer's Comments

The reviewer's and the study author's results were in agreement. Both the study author's and reviewer's analysis detected a statistically significant reduction (p<0.05) in fecundity and a statistically significant (p<0.05) increase in male GSI score at the 0.00012 and 0.0014 mg a.i./L treatment levels compared to the negative control. The reviewer's conclusions based on the OCSPP 890.1350 flowchart are presented in the Executive Summary and Conclusions sections of this DER.

III. REFERENCES

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APPENDIX I. OUTPUT OF REVIEWER'S STATISTICAL VERIFICATION:

test for fish screen study - Cypermethrin ANALYSIS RESULTS FOR VARIABLE VAR01 (F body weight (g))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS
Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01
Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05
Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.913	0.132	1.115	0.381	USE PARAMETRIC TESTS

BASIC ST	JMMA I	RY STATIS	rics				
Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.I	nterval
Ctrl	4	1.39	0.20	0.10	14.28	1.08,	1.71
Dosel	4	1.48	0.13	0.07	8.84	1.27,	1.68
Dose2	4	1.27	0.11	0.05	8.29	1.10,	1.44
Dose3	4	1.26	0.18	0.09	13.92	0.98,	1.54
Level		Median	Min	Max	%of Control (means)	%Reduct	ion(means)
Ctrl		1.32	1.25	1.69			
Dose1		1.47	1.34	1.63	105.83	-5.8	3
Dose2		1.24	1.18	1.41	90.97	9.0	3
Dose3		1.27	1.09	1.44	90.71	9.2	9

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Analysis of Variance (ANOVA) - overall F-test
Numerator df Denominator df F-stat P-value
3 12 1.71 0.218

Dunnett - testing each trt mean signif. different than control Williams - test assumes dose-response relationship, testing negative trend Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett		Williams	Tukey p-values						
		p-value	mean	p-value	Dosel	Dose2	Dose3	Dose4	Dose5		
C+1	1 20		1 43								
Ctrl	1.39		1.43		•		•	•	•		
Dosel	1.48	0.808	1.43	0.727							
Dose2	1.27	0.552	1.27	0.177	0.292						
Dose3	1.26	0.531	1.26	0.175	0.279	1.000			-		

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom TestStat P-value

3 3.86 0.277

```
MannWhit - testing each trt median signif. different from control
Jonckheere - test assumes dose-response relationship, testing negative trend
Level
        Median
                       MannWhit p-value
                                              Jonckheere p-value
 Ctrl
         1.32
 Dosel
          1.47
                               0.494
                                                    0.807
                                                    0.153
 Dose2
          1.24
                               0.346
 Dose3
          1.27
                               0.678
                                                    0.081
DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL
                                        >highest dose (no sign. differences)
  Williams
  Jonckheere
                                        >highest dose (no sign. differences)
***************
PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
   Analysis of Variance (ANOVA) - overall F-test
    Numerator df Denominator df F-stat
                                  1.71
                                            0.218
         3
                   1.2
Dunnett - testing each trt mean signif, different than control
Williams - test assumes dose-response relationship, testing INCREASING trend
Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC
            Dunnett Isotonic Williams
Level
      Mean
                                                    Tukey p-values
                      mean p-value Dosel Dose2 Dose3 Dose4
             p-value
                                                                   Dose5
       -1.39
Ctrl
                       -1.35
Dose1
                             0.737
             0.808
       -1.48
                       -1.35
                                        0.292
Dose2
       -1.27
              0.552
                       -1.35
             0.531
                                     0.279
Dose3
      -1.26
                       -1.35
                               0.788
                                              1.000
NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
   Kruskal-Wallis test - equality among treatment groups
    Degrees of Freedom TestStat P-value
                                 0.277
                        3.86
MannWhit - testing each trt median signif. different from control
Jonckheere - test assumes dose-response relationship, testing INCREASING trend
       Median
                      MannWhit p-value
                                              Jonckheere p-value
Level
         -1.32
 Ctrl
          -1.47
                               0.494
                                                    0.193
 Dose1
                                                    0.847
 Dose2
          -1.24
                               0.346
                                                    0.919
          -1.27
                               0.678
 Dose3
                               LOWEST CONCENTRATION SIGNIF. GREATER THAN CONTROL
```

test for fish screen study - Cypermethrin ANALYSIS RESULTS FOR VARIABLE VAR02 (M body weight (g))

INCREASING TREND TEST SUMMARY

Williams

Jonckheere

>highest dose (no sign. differences)

>highest dose (no sign. differences)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat P-value Test Stat P-value 0.936 0.305 3.162 0.064 USE PARAMETRIC TESTS ************** BASIC SUMMARY STATISTICS StdErr Coef of Var 95% Conf.Interval Level N Mean StdDev Ctrl 4 3.02 0.37 0.19 12.34 2.43, 3.61 Dosel 4 3.57 0.78 0.39 21.91 2.33, 4.81 Dose2 4 3,60 0.31 4.58 0.62 17.10 2.62, 3.18 Dose3 4 0.17 0.09 5.41 2.91, 3.45 Level Median Max %of Control(means) %Reduction(means) Min 2.64 3.44 Ctrl 3.00 2.42 Dose1 3.84 4.17 118.17 -18.17Dose2 3.63 2.93 4.20 119.13 -19.13Dose3 3.19 2.97 3.38 105.26 -5.26PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value 12 1.14 0.373

Dunnett - testing each trt mean signif. different than control Williams - test assumes dose-response relationship, testing negative trend Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett	Isotonic	Williams		Tukey p-values					
		p-value	mean	p-value	Dose1	Dose2	Dose3	Dose4	Dose5		
Ctrl	3.02		3.40								
Dosel	3.57	0.374	3.40	0.895							
Dose2	3.60	0.337	3.40	0.917	1.000				•		
Dose3	3.18	0.953	3.18	0.796	0.739	0.696		•	•		

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom TestStat P-value 3.04 0.385

MannWhit - testing each trt median signif. different from control Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit p-value	Jonckheere p-value
Ctrl	3.00		•
Dose1	3.84	0.346	0.876
Dose2	3.63	0.235	0.928

EPA MRID Number 48683001									
Dose3	3.	19		0.678			0.680		
Willi	SING TRE lams . cheere	ND TEST S	UMMARY	LOWEST CO	>highes	t dose	NIF. LESS (no sign. (no sign.	. differe	ences)
PARAMETE Anal	RIC ANAL	YSES - Variance	use alpha (ANOVA) - ominator d	********** -level=0.09 overall F- f F-sta 1.14	5 for all -test t P		****	*****	***
Williams	- test	assumes	dose-respo	gnif. diffense relationse relationse relationse compari	onship, t	esting	INCREASIN		
Level	Mean	Dunnett p-value		Williams p-value	Dose1	Dose2	Tukey p-v Dose3		Dose5
Dose2	-3.60	0.374 0.337 0.953	-3.02 -3.45 -3.45 -3.45	0.168 0.179 0.186	1.000 0.739	0.696	· · ·	· ·	· · ·
NON-PARA	AMETRIC skal-Wal	ANALYSES	- use a - equality		=0.05 for atment gr	all te		*****	* * *
				signif. di ponse rela				SING tre	nd
Level Ctrl Dosel Dose2 Dose3	-3.	00 84 63	Man nW hi	0.346 0.235 0.678		Jonckh	0.124 0.072 0.320	alue	
Willi		ND TEST S	UMMARY	LOWEST CO	>highes	t dose	NIF. GREA (no sign. (no sign.	. differe	
			dy - Cyper IABLE VARO	methrin 3 (Fbody	y length	(mm))			
Shapiro- Levenes Use para Shapir Test	-Wilks t test fo ametric	est for North	ormality o eity of va if neither -Wilks ue T	C ANALYSIS f Residual: riance(absolutest reject Levenes est Stat 1.347	olute res cted, oth Levenes P-value	iduals) erwise Concl	alpha	metric ar	0.05 nalyses.

*****	****	******		******	******	*****	****	******	***
BASIC SU	·	STATISTI							
Level		Mean	StdDev	\mathtt{StdErr}	Coef of	Var	95% Conf.		
Ctrl		50.81	0.98	0.49	1.93		49.25,		
Dose1	4	49.61	1.15	0.57	2.32		47.78,		
Dose2	4	48.56	0.91	0.46	1.88		47.11,	50.01	
Dose3	4	50.02	2.18	1.09	4.36		46.56,	53.49	
Leve1	Me	edian	Min	Max 9	of Control	(means)	%Reduct	tion (mear	ns)
Ctrl		50.72	49.72	52.10					
Dose1		49.58	48.45	50.83	97.63		2.3	37	
Dose2		48.17	47.99	49.92	95.57		4.4	43	
Dose3		50.83	46.89	51.54	98.45		1.5	55	

PARAMETR			-		0.05 for al	1 tests	•		
	-			- overall		D 1			
Nun	erator	ai I	enominato			P-value	!		
	3		12	I.	,79	0.202			
					ifferent th			1	
					ationship,				
Tukey -	two-sid	ded test	s, all pos	ssible comp	parisons, n	ot used	for NOEC	or LOEC	
Level	Mean	Dunnat	t Isotoni	ic William			Tukey p-	valuee	
rever	Mean	p-valu				Dose2		Dose4	Dose5
		p-vart	e mean	p-varu	le Dosei	DOSEZ	Doses	DOSET	DODCO
Ctrl	50.81		50.83	ı					
Dosel	49.61					•	•	•	•
Dose1 Dose2						•	•	•	•
Dose3						0.480		•	•
Doses	50.02	0.760	49.2	0.05	0.973	0.400		•	•
*****	****	******	*****	*****	******	*****	*****	*****	***
NON-PARA	METRIC	ANALYSE	S - use	e alpha-lev	vel=0.05 fo	r all t	.est s		
Krus	kal-Wa	llis tes	t - equal:	ity among t	treatment g	roups			
Deg	rees o	f Freedo	m TestSi	tat P-va	alue				
_	3		5.0	0.0	.168				
MannWhit	- tes	ting eac	h trt med:	ian signif.	. different	from c	control		
					elationship			ve trend	
				-					
Level	Med	ian	Manni	Whit p-valu	ıe	Jonak	heere p-v	alue	
Ctrl	50	.72							
Dose1	49	.58		0.346			0.124		
Dose2	48	.17		0.103			0.006		
Dose3	50	.83		0.889			0.131		
	·			* AMP		mTON 07	CMIE IEC	C TUNK (*/	TORTRO
		END TEST	SUMMARY	LOWES	r concentra				
Willi							(no sign		
Jonek	heere				>highe	st dose	(no sign	. alliere	ences)
******			*****	*****	*****	*****	*****	******	***

Ana		of Variance	e (ANOVA)	a-level=0.(- overall i df F-sta	-test	tests			
	3		12		9 0				
William	s - tes	st assumes	dose-resp	ignif. difi onse relati ible compar	ferent tha lonship, t	n contr	INCREASIN		
Level	Mean			Williams p-value		Dose2	Tukey p-v Dose3		Dose5
Dose3	-50.02	0.768		0.895	0.719 0.975	0.480		· ·	:
				*****				*****	***
				alpha-level			ests		
				y among tre		oups			
De	_	of Freedom		t P-valu					
	3		. 5.05	0.16	58				
				n signif. o sponse rela				ING tren	d
Level	Med	lian	MannWh	it p-value		Jonekh	eere p-va	lue	
Ctrl	-50	.72							
Dosel	-49	.58		0.346			0.876		
Dose2	-48	3.17		0.103			0.994		
Dose3	-5(,83		0.889			0.869		
Will		REND TEST	SUMMARY	LOWEST (t dose	SNIF. GREA (no sign. (no sign.	differe	nces)
			udy - Cype: RIABLE VAR		du longth	(\ \ \			
				04 (13 20)	ay rength	(mm))			
Shapiro Levenes Use par Shapi	F ASSUM -Wilks test mametric ametric ro-Will	PTIONS FO test for for homoge analyses s Shapir	Normality neity of voithe o-Wilks	IC ANALYSIS of Residual ariance(abs r test rejo Levenes	solute resected, oth	a-level iduals) erwise	alpha	n-level=0 netric an	.05 alyses.
Shapiro Levenes Use par Shapi Tes	F ASSUM -Wilks test mametric ametric ro-Will t Stat	MPTIONS FO test for for homoge analyses s Shapir P-va	Normality neity of voif neithe newilks lue	IC ANALYSIS of Residual ariance(abs r test rejo Levenes Test Stat	solute resected, oth Levenes P-value	a-level iduals) erwise Concl	alpha non-param lusion	netric an	.05 alyses.
Shapiro Levenes Use par Shapi Tes	F ASSUM -Wilks test mametric ametric ro-Will	PTIONS FO test for for homoge analyses s Shapir	Normality neity of voif neithe newilks lue	IC ANALYSIS of Residual ariance(abs r test rejo Levenes	solute resected, oth	a-level iduals) erwise Concl	alpha	netric an	.05 alyses.
Shapiro Levenes Use par Shapi Tes	F ASSUM -Wilks test : ametric ro-Will t Stat .910	MPTIONS FO test for for homoge analyses s Shapir P-va 0.1	Normality neity of voice if neithe o-Wilks lue 18	IC ANALYSIS of Residual ariance(abs r test rejo Levenes Test Stat	is alph solute res ected, oth Levenes P-value 0.597	a-level duals) erwise Concl	alpha non-param lusion PARAMETRIC	netric an	alyses.
Shapiro Levenes Use par Shapi Tes 0	F ASSUM -Wilks test in ametric ro-Will t Stat .910	MPTIONS FO test for for homoge analyses s Shapir P-va 0.1	Normality neity of v if neithe o-Wilks lue 18	IC ANALYSIS of Residual ariance(abs r test rejo Levenes Test Stat 0.652	ls alph solute res ected, oth Levenes P-value 0.597	a-level iduals) erwise Concl USE E	alpha non-param lusion PARAMETRIC	etric an	alyses.
Shapiro Levenes Use par Shapi Tes 0	F ASSUM-Wilks test is ametric ro-Will t Stat .910	PTIONS FO test for for homoge analyses S Shapir P-va 0.1 ***********************************	Normality neity of v if neithe o-Wilks lue 18 *********** S tdDev	IC ANALYSIS of Residual ariance (absortest rejo Levenes Test Stat 0.652	ls alph solute res ected, oth Levenes P-value 0.597	a-level iduals) erwise Concl USE E	alpha non-param lusion PARAMETRIC ************************************	etric and TESTS	alyses.
Shapiro Levenes Use par Shapi Tes 0	F ASSUM-Wilks test is ametric ro-Will t Stat .910	APTIONS FO test for for homoge analyses s Shapir P-va 0.1 ********* STATISTIC Mean S 61.64	Normality neity of v if neithe o-Wilks lue 18 ********* S tdDev 2.27	IC ANALYSIS of Residual ariance (absortest rest Levenes Test Stat 0.652 ************************************	ls alph solute res ected, oth Levenes P-value 0.597 ************************************	a-level iduals) erwise Concl USE E	alpha non-param lusion PARAMETRIC ************************************	TESTS ******* Interval 65.25	alyses.
Shapiro Levenes Use par Shapi Tes 0 ******** BASIC S	F ASSUM -Wilks test if ametric ro-Will t Stat .910 ****** UMMARY N 4 4	PTIONS FO test for for homoge analyses S Shapir P-va 0.1 ***********************************	Normality neity of v if neithe o-Wilks lue 18 *********** S tdDev	IC ANALYSIS of Residual ariance (absortest rejo Levenes Test Stat 0.652	ls alph solute res ected, oth Levenes P-value 0.597	a-level iduals) erwise Concl USE E	alpha non-param lusion PARAMETRIC ************************************	etric and TESTS	alyses.

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Take I F The state of the state							EPA MRID Number 48683001					
Dose 61.78 58.82 64.19 Dose 65.35 58.93 66.63 103.93 -3.93 Dose 62.24 61.31 64.94 101.69 -1.69	Dose3	4 (62.68	1.69	0.84	2.0	69	60.00,	65.37			
Dose 65.35						%of Cont	rol(means)	%Reduc	tion(mea	ns)		
Dose2 64.89 60.91 66.43 104.28 -4.28 Dose3 62.24 61.31 64.94 101.69 -1.69 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value 3 12 Dunnett - testing each trt mean signif. different than control Williams - test assumes dose-response relationship, testing negative trend Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC Level Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dose1 Dose2 Dose3 Dose4 Dose Ctrl 61.64 . 63.33	_					100			0.7			
Dose3 62.24 61.31 64.94 101.69 -1.69							-					
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Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value 3 12 0.88 0.481 Dunnett - testing each trt mean signif. different than control Williams - test assumes dose-response relationship, testing negative trend Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC Level Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4 Dose Ctrl 61.64 . 63.33 Dose1 64.07 0.455 63.33 0.878 Dose2 64.28 0.392 63.33 0.902 0.999 Dose3 62.68 0.900 62.68 0.838 0.880 0.828 NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 2.60 0.457 MannWhit - testing each trt median signif. different from control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit p-value Jonckheere p-value Ctrl 61.78 Dose2 64.89 0.346 0.876 Dose2 64.89 0.346 0.810 Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams Signif Canalysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value	PARAMETE	RTC ANAI	YSES	- use als	nha-level	=0.05 for	all tests					
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Dunnett - testing each trt mean signif. different than control Williams - test assumes dose-response relationship, testing negative trend Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC Level Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4 Dose Ctrl 61.64 . 63.33		_					P-value	ı				
Dunnett - testing each trt mean signif. different than control Williams - test assumes dose-response relationship, testing negative trend Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC Level Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4 Dose Ctrl 61.64 . 63.33	11421		<u> </u>									
Williams - test assumes dose-response relationship, testing negative trend Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC Level Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4 Dose Ctrl 61.64 . 63.33		_					21102					
Dunnett Isotonic Williams Tukey p-values Dose	Williams	s - test	assume	s dose-re	sponse re	lationship	, testing	negative				
Description	Tukey -	TWO-SIG	ded test	s, all pos	ssible co	mparisons,	not used	IOF NOEC	or LUEC			
Description	Level	Mean	Dunnet	t Isotoni	ic Willi	ать		Tukev n-	values			
Ctrl 61.64 . 63.33	20101	110411					1 Dose2			Dose5		
Dosel			P valu		PVG	240 2011	30002	20200	50001			
Dosel	Ctrl	61.64		63.33	3.							
Dose2 64.28 0.392 63.33 0.902 0.999	Dosel											
Dose3 62.68 0.900 62.68 0.838 0.838 0.828						02 0.99			•			
NON-PARAMETRIC ANALYSES — use alpha-level=0.05 for all tests Kruskal-Wallis test — equality among treatment groups Degrees of Freedom TestStat P-value 3 2.60 0.457 MannWhit — testing each trt median signif. different from control Jonckheere — test assumes dose-response relationship, testing negative trend Level Median MannWhit p-value Jonckheere p-value Ctrl 61.78 Dosel 65.35 0.346 0.876 Dose2 64.89 0.346 0.810 Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere >highest dose (no sign. differences) ***********************************												
NON-PARAMETRIC ANALYSES — use alpha-level=0.05 for all tests Kruskal-Wallis test — equality among treatment groups Degrees of Freedom TestStat P-value 3 2.60 0.457 MannWhit — testing each trt median signif. different from control Jonckheere — test assumes dose-response relationship, testing negative trend Level Median MannWhit p-value Jonckheere p-value Ctrl 61.78 Dosel 65.35 0.346 0.876 Dose2 64.89 0.346 0.810 Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere >highest dose (no sign. differences) ***********************************	*****	*****	******	****	*****	*****	*****	*****	*****	***		
Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 3 2.60 0.457 MannWhit - testing each trt median signif. different from control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit p-value Jonckheere p-value Ctrl 61.78 Dosel 65.35 0.346 0.876 Dose2 64.89 0.346 0.810 Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere >highest dose (no sign. differences) ***********************************												
Degrees of Freedom TestStat P-value 3 2.60 0.457 MannWhit - testing each trt median signif. different from control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit p-value Jonckheere p-value Ctrl 61.78 Dosel 65.35 0.346 0.876 Dose2 64.89 0.346 0.810 Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere >highest dose (no sign. differences) ************************************					-							
MannWhit - testing each trt median signif. different from control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit p-value Jonckheere p-value Ctrl 61.78 Dosel 65.35 0.346 0.876 Dose2 64.89 0.346 0.810 Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere >highest dose (no sign. differences) ***********************************				-			3 <u>-</u>					
Level Median MannWhit p-value Jonckheere p-value Ctrl 61.78 Dosel 65.35 0.346 0.876 Dose2 64.89 0.346 0.810 Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere >highest dose (no sign. differences) ***********************************		-										
Level Median MannWhit p-value Jonckheere p-value Ctrl 61.78 Dosel 65.35 0.346 0.876 Dose2 64.89 0.346 0.810 Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere >highest dose (no sign. differences) ***********************************												
Level Median MannWhit p-value Jonckheere p-value Ctrl 61.78 Dosel 65.35 0.346 0.876 Dose2 64.89 0.346 0.810 Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams > highest dose (no sign. differences) Jonckheere > highest dose (no sign. differences) ***********************************												
Ctrl 61.78	Jonckhee	ere - te	est assu	mes dose-	response	relations	nip, testi	ng negati	ve trend			
Ctrl 61.78	T 1	35		Mana	White man	1	Tonale	hoomo n-u	2100			
Dosel 65.35 0.346 0.876 Dose2 64.89 0.346 0.810 Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences)				Mailin	wurc b-Ag	Tue	Jones	meere b-A	arue			
Dose2 64.89 0.346 0.810 Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere >highest dose (no sign. differences) ***********************************					0.34	6		0.876				
Dose3 62.24 0.494 0.610 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences)												
DECREASING TREND TEST SUMMARY Williams Jonckheere *********************************						_						
Williams	Doses	02	. 24		0.42	•		0.010				
Williams	DECREAS	SING TRE	END TEST	SHMMARY	LOWE	ST CONCENT	TRATION SI	GNIF. LES	S THAN C	ONTROL		
Jonckheere >highest dose (no sign. differences) ***********************************			1001	DOITHIN	Lonz							
PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value												
PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value	تــــــــــــــــــــــــــــــــــــ			***		****		*****	*****	***		
Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value												
Numerator df Denominator df F-stat P-value							all tests	1				
							P-waluo	,				
5 12 0.00 0,401	NUN		uı, L					•				
		3		12		0.00	0,401					

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Dunnett - testing each trt mean signif. different than control Williams - test assumes dose-response relationship, testing INCREASING trend

m		1 - 3			,, ,						
Tukey -	TWO	o-sided	tests,	all pos	SIDL	compar	isons, no	t used	for NOE	C or LOEC	;
Level	Me		nnett	Isotoni		illiams			Tukey p		
		P-	value	mean	I	o-value	Dosel	Dose2	Dose3	Dose4	Dose5
Ctrl	-61	1.64		-61.64	l						
				-63.68		0.178					
			.392	-63.68	3	0.190	0.999				
Dose3	-62	2.68	.900	-63 .6 8	l	0.197	0.880	0.828		•	•
****	***	******	****	*****	****	*****	*****	*****	*****	****	***
NON-PARA	AMET	TRIC ANA	LYSES	- use	alph	na-level	=0.05 for	all te	ests		
							eatment gr				
Deg	gree	es of Fr	eedom			P-valu	ie				
		3		2.6	0	0.45	7				
MannWhit	_	testino	each	trt medi	an si	onif d	lifferent	from co	ntrol		
							tionship,			ASING tre	end
					•				_		
Level		Median		MannW	hit p	-value		Joneki	neere p-	value	
Ctrl		-61.78 -65.35			,	. 246			0 104		
		-64.89			-).346).346			0.124 0.190		
		-62.24				0.494			0.390		
00363		02.24			,	7.424			0.390		
INCREAS	SING	TREND	TEST S	UMMARY	I	LOWEST C	ONCENTRAT	ION SIG	NIF. GR	EATER THA	N CONTROL
Willi	iams	3					>highes	t dose	(no sign	n. differ	ences)
Jonel	chee	ere					>highes	t dose	(no sign	n. differ	ences)
test for	. F;	sh care	on stu	dur – Cum	armat	hrin					
							ellogenin	(ng/m]	3 3		
	, ,,,		OI(VIII)	11111111111111111111111111111111111111		(1 +10	.crroger.	· (IIIg/IIII	-, ,		
TESTS OF	: AS	SUMPTIC	NS FOR	PARAMET	RIC A	NALYSIS	3				
							s alph				
							solute res				
							cted, oth			ametric a	malyses.
_			-				Levenes		lusion		
			P-val			: Stat	P-value 0.715		PARAMETR	TC MPCMC	
0.	.941	L	0.36	1	u,	.460	0.715	056 1	ARAMETR.	IC TESTS	
******	***	*****	*****	*****	****	*****	*****	****	****	*****	***
BASIC SU	JMMA	ARY STAT	ISTICS								
Level	N	Mean	St	dDev	Sto	iErr	Coef of V	ar 9	95% Conf	.Interval	
Ctrl	4	117500	0 2629	95.6 1	31497	7.8	22.38		6515.4,		
Dose1		842500.			20718		28.66		8320.4,		
Dose2		111250			85534		33.35		22047.6,		
Dose3	4	105000	0 2886	75.1 1	4433	7.6	27.49	59	90653.4,	1509347	
Level		Media	ın 1	Min	Max	c %of	Control ((means)	%Reduc	ction(mea	ns)
Ctrl			0008 00		14000					,	
Dosel		875000.			11000		71.70		28	.30	
Dose2		103000	0 7900		16000		94.68		5	.32	
Dose3		105000	0 7000	00.0	14000	000	89.36		10	. 64	

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						11171112	- 100000	
********		****						****
PARAMETRIC ANA			-level=0.05					
Analysis o								
Numerator			f F-stat		P-value			
3	1	2	0.96	(0.445			
Dunnett - test: Williams - test Tukey - two-sic	t assumes	dose-respo	nse relatio	onship,	testing	negative		
		_						
Level Mean	Dunnett	Isotonic				Tukey p-		_
	p-value	mean	p-value	Dosel	Dose2	Dose3	Dose4	Dose5
Ctrl 1175000		1175000						
Dose1842500.0		1001667	0.252	-	_			
Dose2 1112500			0.270	0.584				
Dose3 1050000		1001667	0.279	0.755				
20303 1030000	010.3	1001001	0.2,3	01.00	0.,,,	•	,	
******	******	*****	*****	*****	****	****	*****	***
NON-PARAMETRIC	ANALYSES	- use a	lpha-level=	=0.05 for	r all te	ests		
Kruskal-Wa								
	f Freedom		P-value		LUGFU			
3	r rrecdom	2,43	0.488					
•		2,15	0.10					
MannWhit - tes Jonckheere - te	ting each	trt median	signif, di	ifferent	from co	ontrol	ro trend	
oonckneere - c	est assume	s dose-res	ponse rerac	.tonship,	, reserv	ig negaci	ve crema	
Level Med	ian	MannWhi	t p-value		Jonckh	eere p-va	alue	
Ctrl 1250	000							
Dosel 87500	0.0		0.235			0.074		
Dose2 1030	000		0.780			0.304		
Dose3 1050	000		0.580			0.372		
DECREASING TR	END TEST S	UMMARY	LOWEST CO			NIF. LES		
Williams				>highe:	st dose	(no sign	. differ	ences)
Jonckheere				>highe:	st dose	(no sign	. differ	ences)
******	*****	******	*****	****	****	*****	*****	***
PARAMETRIC ANA	LYSES -	use alpha	-level=0.05	for all	l tests			
Analysis o	f Variance	(ANOVA) -	overall F-	-test				
Numerator		ominator d			P-value			
3	1	2	0.96		0.445			
	_	_						
Dunnett - test	ing each t	rt mean si	gnif, diffe	erent tha	an conti	rol		
Williams - tes							NG trend	
Tukey - two-si	ded tests,	all possi	ble compari	isons, n	ot used	for NOEC	or LOEC	
_						multiple = =		
Level Mean	Dunnett	Isotonic	Williams		n	Tukey p-		Door F
	p-value	mean	p-value	Dosel	Dose2	Dose3	Dose4	Dose5
Ctrl -1175000		-1008750		•	-			
Dose1 -842500	0.302	-1008750	0.855	•	•	•	•	

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					EPA	MRID Numb	per 48683001
Dose2-111250 Dose3-105000		31 -1081250 9 -1081250			0.990		· · ·
******	******	*****	*****	*****	****	*****	*****
		est - equali Nom TestSt	_	eatment g ue		ests	
MannWhit - te Jonckheere -							SING trend
Level Me	edian	MannW	hit p-value	•	Jonck	neere p-v	alue
Dosel -87			0.235			0.926	
Dose2 -103			0.780			0.696	
Dose3 -105			0.580			0.628	
INCREASING T Williams Jonckheere		T SUMMARY	LOWEST	>highe	st dose	(no sign	ATER THAN CONTROL . differences) . differences)
test for fish ANALYSIS RESU				tello ge ni	n (ng/ml	5))	
	s test for homo for homo ic analys lks Shap	or Normality ogeneity of	of Residua variance(ab er test rej	ls alp solute re ected, ot Levenes	siduals) herwise Conci	alph	metric analyses.
**************************************			****	*****	*****	*****	****
Level N		StdDev	StdErr	Coef of	Var (95% Conf.	Interval
		33.34	16.67	81.31		-12.05,	
Dosel 4		72.35	36.17	136.50		-62.12,	
	39.25		12.69	64.67		-1.14,	79.64
Dose3 4	35.00	29.13	14.57	83.23		-11.36,	
Level	Median	Min	Max %c	f Control	(means)	%Reduc	tion(means)
Ctrl	38.00	12.00	76.00				
Dosel		12.00	161.00	129.27		-29.	
Dose2	36.50	13.00	71.00	95.73		4.	
Dose3	25.00	13.00	77.00	85.37		14.	63
*****	*****	******	*****	*****	****	*****	****
PARAMETRIC A					l tests		
		nce (ANOVA)			D 1		
Numerato	or df	Denominator			P-value		
3		12	0.1	. 2	0.946		

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Dunnett - testing each trt mean signif. different than control Williams - test assumes dose-response relationship, testing negative trend Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Dose1	Dose2	Tukey p- Dose3	values Dose4	Dose5
Ctrl	41.00		47.00						
Dosel	53.00	0.962	47.00	0.662					
Dose2	39.25	1.000	39.25	0.593	0.970				
Dose3	35.00	0.995	35.00	0.551	0.938	0.999	•	•	

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom TestStat P-value

3 0.49 0.921

MannWhit - testing each trt median signif. different from control Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit p-value	Jonckheere p-value
Ctrl	38.00		
Dosel	19.50	0.887	0.384
Dose2	36.50	1.000	0.588
Dose3	25.00	0.780	0.664

DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL
Williams >highest dose (no sign. differences)
>highest dose (no sign. differences)

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Analysis of Variance (ANOVA) - overall F-test
Numerator df Denominator df F-stat P-value
3 12 0.12 0.946

Dunnett - testing each trt mean signif. different than control Williams - test assumes dose-response relationship, testing INCREASING trend Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett	Isotonic	Williams			Tukey p-	values	
		p-value	mean	p-value	Dosel	Dose2	Dose3	Dose4	Dose5
Ctrl	-41.00		-41.00						•
Dosel	-53.00	0.962	-42.42	0.564					
Dose2	-39.25	1.000	-42,42	0.598	0.970				
Dose3	-35.00	0.995	-42.42	0.617	0.938	0.999	•	•	٠

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom TestStat P-value

					EPA MRID Numbe	er 48683001
	3	0.4	9 0.	921		
MannWhit ~	testing e	each trt medi	an sionif.	different f	rom control	
					testing INCREAS	SING trend
Level	Median	MannW	hit p-valu	e	Jonckheere p-va	ılue
Ctrl	-38.00					
Dosel	-19.50		0.887		0.616	
Dose2	-36.50		1.000		0.412	
Dose3	-25.00		0.780		0.336	
INCREASING Williams		EST SUMMARY	LOWEST		ON SIGNIF, GREA dose (no sign.	TER THAN CONTRO differences)
Jonckhe	ere				dose (no sign.	
		n study - Cyp R VARIABLE VA		SI)		
TESTS OF A	SSUMPTIONS	FOR PARAMET	RIC ANALYS	IS		
		or Normality				
					iduals) alpha	-level=0.05
						etric analyses.
Shapiro-	Wilks Sha	apiro-Wilks	Levenes	Levenes	Conclusion	
Test S	tat 1	-value	Test Stat	P-value		
0.91	0	0.117	1.388	0.294	USE PARAMETRIC	TESTS
*****	*****	****	******	****	*****	****
BASIC SUMM	ARY STATIS	STICS				
Level N	Mean	StdDev	StdErr	Coef of Va	ar 95% Conf.I	nterval
Ctrl 4		4.21	2,11	35.46	5.17,	18.58
Dosel 4			1.09	19.37	7.80,	
	11.20		1.12	20.06	7.63,	
Dose3 4		1.50	0.75	10.53	11.86,	
Level	Median	Min	Max %	of Control(m	neans) %Reduct	cion(means)
Ctrl	10.50	8.50	18.00			
Dosel	11.00	9.10	14.00	94.95	5.0)5
Dose2	10.85	9.10	14.00	94.32	5.6	8
Dose3	14.00	13.00	16.00	120.00	-20.0	00
*****	******	*****	*****	*****	******	*******
PARAMETRIC				.05 for all	tests	
_		lance (ANOVA)			-value	
Numer	ator df 3	Denominator 12			.386	
	J	14	1.		, 20 U	
		ach trt mean				
Williams -	test assu	mes dose-res	ponse rela	tionship, te	esting negative	trend
Tukey - tw	o-sided to	ests, all pos	sible comp	arisons, not	used for NOEC	or LOEC
Level M	ean Duni	nett Isotoni	c William	S	Tukey p-v	_
	p-va	alue mean	p-valu	e Dosel	Dose2 Dose3	Dose4 Dose5

						EPA N	ARID Numb	er 486830	01
					_				_
Ctrl	11.88		12.15	•					
Dosel	11.28		12.15	0.642	•		•	•	•
		0.971	12.15	0.677					•
Dose3	14.25	0.492	12.15	0.696	0.445	0.425	•		•
*****	*****	******		******				*****	***
		ANALYSES		lpha-level:			sts		
			- equality		_	roups			
De	_	Freedom							
	3		3.82	0.28					
MannWhi	t - test	ing each	trt median	signif. d	ifferent	from con	ntrol		
			s dose-resp					ve trend	
Level	Medi	an	MannWhit	p-value		Jonakhe	eere p-va	alue	
Ctrl									
Dose1				1.000			0.558		
Dose2				1.000			0.500		
Dose3	14.	00		0.343		(0.933		
DECREA:		ND TEST S	UMMARY	LOWEST C				S THAN CO	
Jone	kheere				>highe	st dose	(no sign	. differe	ences)
Nu Dunnett	merator 3 - testi	df Den 1 ng each t	(ANOVA) - ominator di 2 rt mean sig dose-respon	F F-sta 1.10 gnif. diffe	t erent th			NG trend	
			all possil						
Level	Mean	Dunnett	Isotonic	Williams			Tukey p-	values	
		p-value	mean	p-value	Dosel	Dose2	Dose3	Dose4	Dose5
C+-1	-11.88		-11.45						
Ctrl	-11.28	0.979	-11.45	0.673	•	•	•		
	-11.20		-11.45	0.708	1.000	•	•		·
	-11.25		-14.25			0.425	· ·		
							•		
		******** ANALYSES	- 1150 2	********* lpha-level				*****	***
			 equality 	-					
		Freedom	TestStat			•			
0	3		3.82	0.28					
MannWhi Jonckhe	t – test ere – te	ing each est assume	trt median s dose-resp	signif. d ponse rela	ifferent tionship	from com, testing	ntrol g INCREA	SING tre	nd
Level Ctrl	Medi -10.		MannWhit	t p-value		Jonakh	eere p-v	alue	

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						EPA	MRID Numbe	r 486830	01
Dose1 Dose2 Dose3	-11. -10. -14.	85		1.000 1.000 0.343			0.442 0.500 0.067		
Willi		ND TEST	SUMMARY	LOWEST	>highes	t dose	GNIF. GREAS (no sign. (no sign.	differe	ences)
			tudy – Cypo ARIABLE VAI	ermethrin RO8 (M GS	I)				
Shapiro- Levenes Jse para Shapir Test	Wilks t test fo metric	est for homogonanalyse Shapi	Normality eneity of s if neith	RIC ANALYSI of Residua variance(ab er test rej Levenes Test Stat	ls alph solute res ected, oth Levenes P-value	iduals; erwise Conc) alpha non-param	etric a	
٠.	3,0	٠.	723	2.333	0.103	001		+2015	
*****	*****	*****	*****	******	*****	****	******	*****	***
BASIC SU	MMARY S	TATISTI	CS						
Level			StdDev	StdErr	Coef of V	ar	95% Conf.I	nterval	
Ctrl	4	1.11	0.25	0.12	22.28		0.71,	1.50	
	4			0.09	14.72		0.93,	1.51	
Dose2	4	1.35	0.18 0.06	0.03	4.28		1.26,	1.44	
Dose3	4	1.40	0.18	0.09	13.04		1.11,		
Level	Me	dian	Min	Max %o	f Control(means)	%Reduct:	ion(mea	ns)
Ctrl		1.09	0.84	1.40					
Dose1		1.25	0.98	1.40	110.41		-10.4	1	
Dose2		1.35	1,30	1.40	122.17		-22.1	7	
Dose3		1.40	1.20	1.60	126.70		-26.7		
*****	*****	*****	******	*****	*****	*****	*****	****	***
PARAMETE			_	ha-level=0.		tests			
Anal	ysis of			- overall					
Nun	erator 3	df D	enominator	df F-st		-value .143			
		. 1					1		
Williams	- test	assume	s dose-res	signif, dif ponse relat sible compa	ionship, t	esting	negative	trend or LOEC	
Level	Mean	Dunnet	t Isotoni	c Williams			Tukey p-v	alues	
30.01		p-valu		p-value		Dose2			Dose5
	1.11		1.27						
Ctrl		0.700							
		0.700				-	-		
Dosel		0 192	1 27	0.955	() . 740				
	1.35	0.182			0.740 0.515	0.978		•	•

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NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

							- Tourne		
V-11	ukal-Wal	lia tost			atmont a				
				among trea P-value		roups			
nec	•	Freedom	4.28						
	3		4.20	0,23	3				
MannWhit	- test	ing each	trt median	signif. d	ifferent	from co	ntrol		
Jonakhee	ere - te	st assume:	s dose-res	ponse rela	tionship.	. testin	g negati	ve trend	
0011011110				p 01,00			y y		
Level			MannWhi	t p-value		Jonckh	eere p-v	alue	
Ctrl	1.	09							
Dosel	1.	25		0.575			0.769		
Dose2				0.222			0.959		
Dose3	1.	40		0.190			0.982		
DECREAG	TNC TOE	ND TEST S	IIIMADV	LOWEST C	ONCENTER	TON STO	MIE IES	с тнам с	ONTROI.
Willi		NO TEST S	OPMARI	TOMEST C			(no sign		
	cheere						(no sign		
OOHE	(Heere				> ningne.	56 0000	(no bign	. 022202	
*****	*****	*****	*****	*****	****	****	******	*****	****
PARAMETE	RIC ANAL	YSES -	use alpha	-level=0.0	5 for all	l tests			
				overall F					
	nerator			f F-sta		P-value			
	3	1	2	2.18	(0.143			
				gnif, diff					
Williams	s - test	assumes	dose-respo	nse relati	onship,	testing	INCREASI	NG trend	
Tukey -	two-sid	ed tests,	all possi	ble compar	isons, no	ot used	for NOEC	or LOEC	
Level	Mean			Williams			Tukey p- Dose3		Dose5
		p-varue	mean	p-value	Doser	DOSEZ	Duses	DOSCI	Doges
Ctrl	-1.11		-1.11						
Dosel	~1 22	0.700	-1.22	0.229					
Dose2	-1.35	0.182	-1.35	0.048	0.740				
		0.095		0.024		0.978			
				*****				*****	***
				lpha-level			sts		
Krus	skal-Wal	lis test		among tre		roups			
Deg	grees of	Freedom			_				
	3		4.28	0.23	3				
				-115 1	1.5.5	£	1		
MannWhit	t – test	ing each	trt median	signif. d	lirerent	irom co	OUCLOT	STNC Fro	nd
Jonckhee	ere - te	st assume	s dose-res	ponse rela	riousuip	, testi	IG INCKER		iid
Level	Medi	an an	MannWhi	t p-value		Jonekh	eere p-v	alue	
Ctrl	-1.		Plattimit	c p varue		oonex.	.ccic p	4140	
Dosel				0.575			0.231		
Dose2	-1.			0.222			0.041		
Dose3		-		0.190			0.018		
20060									
INCREAS	SING TRE	ND TEST S	UMMARY	LOWEST C	ONCENTRA	TION SIG	NIF. GRE	ATER THA	N CONTROL
Will:			-		Dose2				
	khoore				Dose2				

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Dose2

Jonckheere

```
test for fish screen study - Cypermethrin
ANALYSIS RESULTS FOR VARIABLE VAR09 ( F tubercle score (median) )
TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS
Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01
Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05
Use parametric analyses if neither test rejected, otherwise non-parametric analyses.
 Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion
   Test Stat P-value Test Stat P-value
                                               NO DATA FOR TEST
*************
BASIC SUMMARY STATISTICS
Level N Mean StdDev StdErr Coef of Var 95% Conf.Interval
                             0.00
 Ctrl 4
           0.00
                   0.00
                                       .
 Dosel 4
            0.00
                    0.00
                              0.00
                    0.00
 Dose2 4
Dose3 4
           0.00
                             0.00
                              0.00

        Median
        Min
        Max
        % of Control (means)
        % Reduction (means)

        0.00
        0.00
        0.00
        .
        .

        0.00
        0.00
        .
        .
        .

Level
 Ctrl
 Dosel
            0.00
 Dose2
                    0.00
                             0.00
            0.00
 Dose3
                    0.00
                              0.00
***********
PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
   Analysis of Variance (ANOVA) - overall F-test
    Numerator df Denominator df F-stat
                                             P-value
                . 1 .
                                 ٠
Dunnett - testing each trt mean signif. different than control
Williams - test assumes dose-response relationship, testing negative trend
Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC
            Dunnett Isotonic Williams
                                                     Tukey p-values
Level Mean
              p-value mean p-value Dosel Dose2 Dose3 Dose4
                                                                     Dose5
Ctrl
       0.00
       0.00
 Dosel
 Dose2
        0.00
        0.00
 Dose3
*************
NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
   Kruskal-Wallis test - equality among treatment groups
    Degrees of Freedom TestStat P-value
                         0.00
                                  1.000
```

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MannWhit - testing each trt median signif, different from control

Jonckheere - test assumes dose-response relationship, testing negative trend

Level Median MannWhit p-value Jonckheere p-value Ctrl 0.00 Dosel 0.00 1.000 Dose2 0.00 1.000 Dose3 0.00 1.000 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN Williams Dosel Jonckheere Dosel PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value . 1	
Ctrl 0.00 Dosel 0.00 1.000 Dose2 0.00 1.000 Dose3 0.00 1.000 Dose3 0.00 1.000 Dose3 0.00 1.000 Dose1 Dose3 0.00 1.000 Dose1 Dose1 Dose1 Dose1 Dose1 Dose1 Dose1 Dose1 Dose1 Dose1 Dose1 Dose1 Dose2 Dose3 Dose3 Dose4 Ctrl 0.00	
Ctrl 0.00	
Dose2 0.00 1.000 . Dose3 0.00 1.000 . DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN Williams Dosel Jonckheere Dose1 ARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value	
Dose2 0.00 1.000 . Dose3 0.00 1.000 . DOSECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN Williams Dosel Jonckheere Dosel ***********************************	
Dose3 0.00 1.000 . DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN Williams Dosel Jonckheere Dosel ***********************************	
DECREASING TREND TEST SUMMARY Williams Jonckheere Dosel MARY Milliams Jonckheere Dosel MARY MARY MARY Dosel Dosel MARY MARY	
Williams Jonckheere Dosel ***********************************	
Jonckheere Dosel ***********************************	CONTROI
Jonckheere Dosel ***********************************	
ARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value	
ARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value	
Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value 1	****
Numerator df Denominator df F-stat P-value	
nnnett - testing each trt mean signif. different than control illiams - test assumes dose-response relationship, testing INCREASING tren ikey - two-sided tests, all possible comparisons, not used for NOEC or LOE evel Mean Dunnett Isotonic Williams Tukey p-values	
Innett - testing each trt mean signif. different than control Illiams - test assumes dose-response relationship, testing INCREASING trem ikey - two-sided tests, all possible comparisons, not used for NOEC or LOE ivel Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4	
Illiams - test assumes dose-response relationship, testing INCREASING tremskey - two-sided tests, all possible comparisons, not used for NOEC or LOE evel Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4	•
Illiams - test assumes dose-response relationship, testing INCREASING tremskey - two-sided tests, all possible comparisons, not used for NOEC or LOE evel Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4	
Illiams - test assumes dose-response relationship, testing INCREASING tremskey - two-sided tests, all possible comparisons, not used for NOEC or LOE evel Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4	
evel Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4	
evel Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4	
p-value mean p-value Dosel Dose2 Dose3 Dose4	C .
p-value mean p-value Dosel Dose2 Dose3 Dose4	
trl 0.00	
, , , , , , , , , , , , , , , , , ,	Dose
	•
Dosel 0.00	•
Dose2 0.00	
ose3 0.00	•
***************	****
ON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests	
Kruskal-Wallis test - equality among treatment groups	
Degrees of Freedom TestStat P-value	
3 0.00 1.000	
3 0.00 1.000	
annWhit - testing each trt median signif. different from control	
onckheere - test assumes dose-response relationship, testing INCREASING tr	end
medicale case assumes and temporise relationship, contains and a	
evel Median MannWhit p-value Jonckheere p-value	
Ctrl 0.00	
Dosel 0.00 1.000 .	
Dose2 0.00 1.000 .	
Dose3 0.00 1.000 .	
DOSES V.00 1.000 .	
INCREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. GREATER TH	AN CONT
Williams Dose1	
Jonckheere Dosel	
JUNICANEERE DOSET	
est for fish screen study - Cypermethrin	
NALYSIS RESULTS FOR VARIABLE VAR10 (M tubercle score (median))	
WHISTS MESONIS FOR AWKINGTO AWKID. (W ERDSTOTS SCOTS (WEGIGN))	
CTC OF ACCUMPTIONS FOR REPAREMENTS ANALYSIS	
STS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS	

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat P-value Test Stat P-value 0.967 0.782 1.418 0.286 USE PARAMETRIC TESTS ************ BASIC SUMMARY STATISTICS Level N Mean StdDev StdErr Coef of Var 95% Conf.Interval Ctrl 4 32.50 2.08 1,04 6.41 29.19, 35.81 Dosel 4 37.75 5.91 2.95 15.65 28.35, 47.15 Dose2 4 32.25 4.65 39.64 2.32 14.41 24.86, Dose3 4 26.50 4.51 2.25 17.02 19.32, 33.68 Level Median Max %of Control(means) %Reduction(means) Min Ctrl 32.50 30.00 35.00 Dose1 37.00 32.00 45.00 116,15 -16.15Dose2 33.00 26.00 37.00 99.23 0.77 Dose3 25.00 23.00 33.00 81.54 18.46 ******************* PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value 4.16 3 12 0.031

Dunnett - testing each trt mean signif. different than control Williams - test assumes dose-response relationship, testing negative trend Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Dose1	Dose2	Tukey p-v Dose3	values Dose4	Dose5
Ctrl	32.50		35.13						
Dose1	37.75	0.279	35.13	0.861				•	
Dose2	32.25	1.000	32.25	0.584	0.353				
Dose3	26.50	0.194	26.50	0.053	0.019	0.318		•	•

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Kruskal-Wallis test - equality among treatment groups

Degrees of Freedom TestStat P-value

Degrees of Freedom TestStat P-value 3 6.34 0.096

MannWhit - testing each trt median signif. different from control Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit p-value	Jonckheere p-value
Ctrl	32.50		
Dose1	37.00	0.283	0.904
Dose2	33.00	1.000	0.559
Dose3	25.00	0.190	0.055

DECREASING TRE Williams Jonckheere	ND TEST SUMMAR	Y LOWEST		st dose	GNIF. LES (no sign (no sign	. differ	ences)
***************** PARAMETRIC ANAL Analysis of Numerator 3	YSES - use Variance (ANO	alpha-level=0.	05 for all f-test at I		******	*****	***
Dunnett - testi Williams - test Tukey - two-sid	assumes dose-	response relat	ionship,	testing	INCREASI		
Level Mean		onic Williams an p-value		Dose2	Tukey p-	values Dose4	Dose5
Ctrl -32.50 Dosel -37.75 Dose2 -32.25 Dose3 -26.50		.25 0.616 .25 0.651	0.353 0.019	0.318		· · ·	· · ·
	ANALYSES - lis test - equ Freedom Tes	use alpha-leve	el=0.05 for eatment grave	r all te		****	***
MannWhit - test Jonckheere - te						SING tre	nd
Level Medi Ctrl -32.	50	nnWhit p-value		Jonckh	neere p-v	alue	
Dose1 -37. Dose2 -33. Dose3 -25.	00	0.283 1.000 0.190			0.096 0.441 0.945		
INCREASING TRE Williams Jonckheere	ND TEST SUMMAR	Y LOWEST		st dose	NIF. GRE. (no sign (no sign	. differ	ences)
test for fish s ANALYSIS RESULT			indity)				
TESTS OF ASSUMP Shapiro-Wilks t Levenes test fo Use parametric Shapiro-Wilks Test Stat 0.953	est for Normal r homogeneity	ity of Residua of variance(ab ither test rej	ls alph solute res	siduals) herwise Concl	alph	metric a	0.05 nalyses.

					E	PA MRID Numb	er 48683001
****					*******		
		RY STATIST		*****	**********	**********	******
Level		Mean	StdDev	StdErr	Coef of Var	95% Conf.I	interval
		14.25		1.49	20.95	9.50.	
		13.50		1.50	22.22	8.73,	
		8.28		2.37	57.20	0.74,	
		2.23		0.44	39.42	0.83,	
Level		Median	Min	Max	of Control(mean	s) %Reduct	ion(means)
Ctrl		14.00	11.00	18.00			
Dose1		13.00	11.00	17.00	94.74	5.2	26
Dose2		7.10	3.90	15.00	58.07	41.9	93
Dose3		2.20	1.30	3.20	15.61	84.3	39
****	****	*****	******	******	******	*****	******
PARAMETI	RIC A	ANALYSES	- use al	pha-level=0	0.05 for all tes	ts	
Ana.	lysis	s of Varia	nce (ANOVA) - overall	. F-test		
Nur	merat	or df	Denominato	r df F-s	stat P-val	.ue	
	3	3	12	12	.001		
		_		-	fferent than co		trend
Tukey -	two-	-sided tes	ts, all po	ssible comp	parisons, not us	ed for NOEC	or LOEC
Level	Mea	an Dunne p-val			_	Tukey p-v se2 Dose3	values Dose4 Dos

Level Mean		Dunnett	Isotonic	Williams	Tukey p-values					
		p-value	mean	p-value	Dosel	Dose2	Dose3	Dose4	Dose5	
Ctrl	14.25		14.25							
Dosel	13.50	0.975	13.50	0.442						
Dose2	8.28	0.054	8.28	0.013	0.151					
Dose3	2.23	<.001	2.23	<.001	0.002	0.083				

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups
Degrees of Freedom TestStat P-value

3 10.65 0.014

MannWhit - testing each trt median signif. different from control Jonckheere - test assumes dose-response relationship, testing negative trend

Median	MannWhit p-value	Jonckheere p-value
14.00		
13.00	0.775	0.328
7.10	0.190	0.032
2.20	0.067	<.001
	14.00 13.00 7.10	14.00

DECREASING TREND TEST SUMMARY
Williams
Dose2
Jonckheere
Dose2

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

	lysis o merator 3	df Den	(ANOVA) - ominator d 2		at	P-value <.001			
William	s - tes	t assumes	rt mean si dose-respo all possi	nse relat:	ionship,	testing	INCREASI		
Level	Mean	Dunnett p-value	Isotonic mean		Dosel	Dose2	Tukey p-	values Dose4	Dose5
Dose1 Dose2	-8.28	0.975 0.054 <.001	-9.56		0.151		: : :	:	· ·
NON-PAR Kru	AMETRIC skal-Wa	ANALYSES	********* - use a - equality TestStat 10.65	lpha-leve among tre P-val	l=0.05 fc eatment g ue	r all te		*****	***
			trt median s dose-res					SING tren	nd
Level Ctrl Dosel Dose2 Dose3	-14 -13 -7	.00 .10	MannWhi	t p-value 0.775 0.190 0.067		Joncki	0.672 0.968 1.000	alue	
Will	SING TR iams kheere	end test s	UMMARY	LOWEST	>highe	st dose	GNIF. GRE (no sign (no sign	. differe	ences)
			dy - Cyper HABLE VAR1		ilíty)				
Shapiro Levenes Use par Shapi Tes	-Wilks test f	test for N or homogen analyses		of Residua riance(ab test rej	ls alp solute re ected, ot Levenes	esiduals) therwise Conci	ı alph	metric ar	0.05 nalyses.
*****	****	*****	*****	*****	*****	****	*****	******	***
BASIC S Level Ctrl Dosel Dose2 Dose3	N 4 4	96.50 97.75	dDev 4.36 0.50 1.73 6.65	StdErr 2.18 0.25 0.87 3.33	Coef of 4.52 0.51 1.79 7.21	Var 9	95% Conf. 89.56, 96.95, 93.74, 81.67,	103.44 98.55	

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Ctrl	Level	Median	Mín	Max %o	f Control	(means)	%Reduc	tion(mea	na)
Dose1						(
Dose2					101.30		-1.	30	
Dose3 94.00 83.00 98.00 95.60 4.40 **PARMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value 3 12 1.39 0.292 **Parmetric testing each trt mean signif. different than control **Parmetric testing each trt mean signif. different than control **Parmetric testing each trt mean signif. different than control **Parmetric testing each trt mean signif. different than control **Parmetric testing each trt mean possible comparisons, not used for NOEC or LOEC **Parmetric Mean Dunnett Isotonic Williams Tukey p-values posed Dose2 Dose3 Dose4 Dose2 **Parmetric testing each trt mean possible comparisons, not used for NOEC or LOEC **Parmetric testing each trt mean possible comparisons, not used for NOEC or LOEC **Parmetric testing each trt mean possible comparisons, not used for NOEC or LOEC **Parmetric testing each trt mean possible comparisons, not used for NOEC or LOEC **Parmetric testing each trt mean possible comparisons, not used for NOEC or LOEC **Parmetric testing each trt mean possible comparisons, not used for NOEC or LOEC **Parmetric testing each trt mean signif different from control concherer test assumes dose-response relationship, testing negative trend **Parmetric Median MannWhit p-value Jonckheere p-value **Parmetric testing each trt median signif different from control concherer test assumes dose-response relationship, testing negative trend **Parmetric Median MannWhit p-value Jonckheere p-value **Parmetric testing test Summary LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams Soloned Parmetric (ANOVA) ocean Soloned Parmetric Produce (ANOVA) ocean Soloned Parmetric Produce (NOVA) ocean Soloned Produce Produce Produce Produce Produce Produce Produce Produce Produce	Dose2								
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ARAMETRIC ANALYSES — use alpha—level=0.05 for all tests Analysis of Variance (ANOVA) — overall F-test Numerator df Denominator df F-stat P-value 3 12 1.39 0.292 Dunnett — testing each trt mean signif. different than control filliams — test assumes dose—response relationship, testing negative trend fukey — two-sided tests, all possible comparisons, not used for NOEC or LOEC devel Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel									
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Numerator df Denominator df F-stat P-value 1.39 0.292 Dunnett - testing each trt mean signif. different than control filliams - test assumes dose-response relationship, testing negative trend takey - two-sided tests, all possible comparisons, not used for NOEC or LOEC devel Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4 Dose Dose2 Pose3 Dose4 Dose Dose2 Pose3 Dose4 Dose Pose2 Pose3 Dose4 Dose Pose2 Pose3 Dose4 Dose Pose2 Pose3 Pose3 Dose4 Dose Pose2 Pose3 Pose3 Pose4 Dose Pose3 Pose4 Dose Pose3 Pose4 Pose5 P						l tests			
Dunnett - testing each trt mean signif. different than control filliams - test assumes dose-response relationship, testing negative trend tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC mevel Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4 Dose Dose2 Dose3 Dose4 Dose5 Dose5 Dose5 Dose5 Dose6 Dose7 Dose7 Dose6 Dose7 Dose8 Dose7 Dose8 Dose7 Dose8 D		_							
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Alliams - test assumes dose-response relationship, testing negative trend takey - two-sided tests, all possible comparisons, not used for NOEC or LOEC devel Mean Dunnett Isotonic Williams Tukey p-values p-value mean p-value Dosel Dose2 Dose3 Dose4 Dose Dose2 Dose3 Dose4 Dose Dose2 Pose3 Dose4 Dose Dose2 Pose5 Dose6 Pose6 Dose6 Pose6 Dose6 Pose6 Dose6 Pose6 Dose6 Pose7 Dose7 Pose7 Dose7 Pose7 Dose7 Pose7 Dose7 Pose7 Dose7 Pose7 Dose7 Dose6 Pose7 Dose7 Dose7 Pose7 Dose7 Dose7 Dose7 Pose7 Dose7 D		3	12	1.3	9	0.292			
Mean Dunnett Isotonic Williams Tukey p-values	Williams	s - test assum	es dose-re	sponse relat	ionship,	testing	negative		
P-value mean p-value Dose1 Dose2 Dose3 Dose4 Dose5	_			-					
Dosel 97.75 0.947 97.13 0.672	Level	Mean Dunne	tt Isoton	ic Williams				values	
Dosel 97.75 0.947 97.13 0.672		p-val	ue mean	p-value	Dosel	Dose2	Dose3	Dose4	Dose5
Dosel 97.75 0.947 97.13 0.672		0.5		_					
Dose2 96.50 1.000 96.50 0.618 0.972	-					•		•	
Dose3 92.25 0.358 92.25 0.108 0.275 0.481					•		•	•	•
CON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 3 4.32 0.229 MannWhit - testing each trt median signif. different from control Monckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit p-value Jonckheere p-value Ctrl 98.50 . Dosel 98.00 0.555 0.219 Dose2 97.00 0.407 0.053 Dose3 94.00 0.281 0.010 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams > highest dose (no sign. differences) Jonckheere Dose3 ***********************************									
NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 3 4.32 0.229 MannWhit - testing each trt median signif. different from control Monckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit p-value Jonckheere p-value Ctrl 98.50	Dose3	92.25 0.35	92.2	5 0.108	0.275	0.481	•	•	•
NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 3 4.32 0.229 MannWhit - testing each trt median signif. different from control Monckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit p-value Jonckheere p-value Ctrl 98.50	*****	******	*****	******	*******	******	******	*****	***
Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 3 4.32 0.229 MannWhit - testing each trt median signif. different from control Monckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit p-value Jonckheere p-value Ctrl 98.50 Dosel 98.00 0.555 0.219 Dose2 97.00 0.407 0.053 Dose3 94.00 0.281 0.010 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams	NON-PARA	METRIC ANALYS	ES - 1186	alpha-leve	1=0 05 fo	r all to	ests		
Degrees of Freedom TestStat P-value 3									
MannWhit - testing each trt median signif. different from control Monckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit p-value Jonckheere p-value Ctrl 98.50 Dosel 98.00 0.555 0.219 Dose2 97.00 0.407 0.053 Dose3 94.00 0.281 0.010 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere Dose3 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value					_	20062			
Level Median MannWhit p-value Jonckheere p-value Ctrl 98.50 Dosel 98.00 0.555 0.219 Dose2 97.00 0.407 0.053 Dose3 94.00 0.281 0.010 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere Dose3 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value	,								
Level Median MannWhit p-value Jonckheere p-value Ctrl 98.50 Dosel 98.00 0.555 0.219 Dose2 97.00 0.407 0.053 Dose3 94.00 0.281 0.010 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere Dose3 PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value									
Ctrl 98.50								ve trend	
Dosel 98.00 0.555 0.219 Dose2 97.00 0.407 0.053 Dose3 94.00 0.281 0.010 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Jonckheere Dose3 ***********************************	Level	Median	Manni	Whit p-value		Jonek	heere p-va	alue	
Dose2 97.00 0.407 0.053 Dose3 94.00 0.281 0.010 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams >highest dose (no sign. differences) Dose3 ***********************************	Ctrl	98.50							
Dose3 94.00 0.281 0.010 DECREASING TREND TEST SUMMARY LOWEST CONCENTRATION SIGNIF. LESS THAN CONTROL Williams > highest dose (no sign. differences) Dose3 ***********************************	Dosel	98.00							
DECREASING TREND TEST SUMMARY Williams Jonckheere Dose3 ***********************************	Dose2	97.00							
Williams >highest dose (no sign. differences) Jonckheere Dose3 ***********************************	Dose3	94.00		0.281			0.010		
Williams >highest dose (no sign. differences) Jonckheere Dose3 ***********************************	beones.	TNO MDEND MEG	m cusas DV	LOMESE	CONCENTING	TTON ST	CNIE IEC	e Tuan C	ገለምምስT
Jonckheere Dose3 ***********************************			I SUMMARI	TOMESI					
**************************************					-	st dose	(no sign	. diller	encesi
PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value	Jones	MEETE			DOSES				
Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value	*****	*****	*****	*****	******	*****	*****	*****	***
Analysis of Variance (ANOVA) - overall F-test Numerator df Denominator df F-stat P-value	PARAMETE	RIC ANALYSES	- use al	pha-level=0.	05 for al	l tests			
Numerator df Denominator df F-stat P-value									
						P-value			
		3			9	0.292			

Dunnett - testing each trt mean signif. different than control Williams - test assumes dose-response relationship, testing INCREASING trend Tukey - two-sided tests, all possible comparisons, not used for NOEC or LOEC

Level	Mean	Dunnett	Isotonic	Millia-			mukan sa	luod	
reser	mean	p-value	mean	p-valu		Dose2	Tukey p- Dose3	Dose4	Dose5
		p varae	nicari	b vare	ie boaei	DOSCE	50303	00004	20000
Ctrl	-96.50		-95.75						
Dosel	-97.75	0.947	-95.75	0.688					
Dose2	-96.50	1.000	-95.75	0.723	0.972				
Dose3	-92.25	0.358	-95.75	0.742	0.275	0.481			
			*****					*****	****
		ANALYSES		-	rel=0.05 fc		ests		
			- equality	_	_	roups			
⊅e	grees of	f Freedom	TestStat 4.32		.229				
	,		4.32	0.	. 229				
MannWhi	t - test	ting each	trt median	gianif	different	from co	ntrol		
			s dose-res					SING tre	n d
						,			
Level	Med:	ian	MannWhi	t p-valu	ie	Jonakh	eere p-v	alue	
Ctrl		.50							
Dose1				0.555			0.781		
Dose2	_			0.407			0.947		
Dose3	-94	.00		0.281			0.990		
				-					
		END TEST S	SUMMARY	LOWEST	CONCENTRA				
Will	ıams kheere						(no sign		
JOHE	rueere				>nighe	st dose	(no sign	. direc	ences)
test fo	r fish s	screen sti	idy - Cyper	methrin					
			RIABLE VAR1		estosteron	e (ng/mI	2))		
							•		
TESTS O	F ASSUM	PTIONS FOR	PARAMETRI	C ANALYS	SIS				
Shapiro	-Wilks 1	test for N	Normality o	f Residu	als alp	ha-level	L=0.01		
Levenes	test fo	or homoger	eity of va	riance(a	absolute re	esiduals)	alph		
			if neither					metric a	nalyses.
		•	-Wilks				lusion		
Tes	t Stat	P-val	lue T	est Stat	r P-value				
					•	NO DA	TA FOR T	EST	
				*****	*******	******	*****	*****	***
DACTO C	ITMMADV (STATISTICS							
Level				StdErr	Coef of	Var (95% Conf.	Interval	
Ctrl	0					,			
Dosel		•							
Dose2							. ,		
Dose3		•		•			. ,		
Level	Me	edian	Min	Max 9	of Control	(means)	%Reduc	tion(mea	ns)
Ctrl			•				•		
Dosel			•						
Dose2		•		•	•				
Dose3			•	•					

```
PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
   Analysis of Variance (ANOVA) - overall F-test
   Numerator df Denominator df F-stat P-value
                               1.39
                                         0.292
        3
                 12
MannWhit - testing each trt median signif. different from control
Jonckheere - test assumes dose-response relationship, testing negative trend
                    MannWhit p-value
                                          Jonckheere p-value
Level
       Median
 Ctrl
 Dosel
 Dose2
 Dose3
  Jonckheere
                                     Dose1
***********
PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
   Analysis of Variance (ANOVA) - overall F-test
    Numerator df Denominator df F-stat
                                         P-value
                               1.39
                                         0.292
        3
                 12
MannWhit - testing each trt median signif. different from control
Jonckheere - test assumes dose-response relationship, testing INCREASING trend
                                          Jonckheere p-value
Level
       Median
                    MannWhit p-value
 Ctrl
 Dosel
 Dose2
 Dose3
  Jonckheere
                                     Dose1
test for fish screen study - Cypermethrin
ANALYSIS RESULTS FOR VARIABLE VARI4 ( M testosterone (ng/mL) )
TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS
Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01
Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05
Use parametric analyses if neither test rejected, otherwise non-parametric analyses.
 Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion
Test Stat P-value Test Stat P-value
                                           NO DATA FOR TEST
*******************
BASIC SUMMARY STATISTICS
Level N Mean StdDev StdErr Coef of Var 95% Conf.Interval
          Mean -
 Ctrl 0
                          .
 Dosel 0
 Dose2 0
 Dose3 0
         Median Min Max %of Control(means) %Reduction(means)
Level
 Ctrl
           .
                  .
```

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					EPA MRID Number 48683001
Dosel					•
Dose2	•		•	•	•
Dose3		•			•
*******	******	******	****	*****	******
PARAMETRI	C ANALYSES	- use al	pha-level=0	.05 for all	tests
		ance (ANOVA			
_	rator df		r df F-s		-value
	3	12	1.3	39 0.	. 292
					from control
Jonckheer	e – test as	sumes dose-	response re	lationship,	testing negative trend
Level	Median	Mann	Whit p-value	€	Jonckheere p-value
Ctrl			•		
Dose1			•		
Dose2	•		•		•
Dose3	•			1	•
Jonekh	eere			Dose1	
******	******	*****	******	*****	*******
PARAMETRI	C ANALYSES	- use al	pha-level=0	.05 for all	tests
		ance (ANOVA	-		
_	rator df		r df F-s		-value
	3	12	1.	39 0.	.292
					from control testing INCREASING trend
Level	Median	Mann	Whit p-value	e	Jonckheere p-value
Ctrl					
Dosel					
Dose2					•
Dose3					•
Jonckh	eere			Dose1	
		study - Cy R VARIABLE V		7b-estradio	l (ng/mL))
Shapiro-W Levenes t Use param Shapiro	ilks test fest for hometric analy- -Wilks Sha	ogeneity of	y of Residu variance(a her test re Levenes Test Stat	als alpha bsolute res jected, othe Levenes P-value	a-level=0.01 iduals) alpha-level=0.05 erwise non-parametric analyses. Conclusion
			•		NO DATA FOR TEST
	**************************************		*****	*****	*******
Level N	Mean	StdDev	StdErr	Coef of Va	ar 95% Conf.Interval
	0 .			•	. , .
Dose1	•		•	•	. , .
Dose2					. ,

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						EPA N	ARID Number 4868	3001
Dose3	O	•	•	•	•		. , .	
Level	1	Median	Min	Max	%of Contro	ol(means)	%Reduction(me	eans)
Ctrl								
Dosel							•	
Dose2			•					
Dose3		•						
*****	****	******	*****	*****	****	******	*****	****
PARAMETE	RIC ANA	ALYSES	- use al	pha-leve	1=0.05 for a	all tests		
Anal	vsis o	of Varia	nce (ANOVA) - over	all F-test			
	ieratoi		Denominato		F-stat	P-value		
	3		12			0.292		
	3		12		1.05	01232		
MannWhit	- te	sting ea	ch trt med	lian sign	if. differer	it from cor	nt rol	
							g negative tre	nd
OUTCATIEC	:re - (test ass	unes dose-	response	Teracronsin	ip, testing	negacive cro.	
Level	Med	dian	Mann	Whit p-va	alue	Jonekhe	eere p-value	
Ctrl	,,,,,	22.011	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	marc p vi	4140	001101111	3020 F 10220	
Dose1		•		•			•	
Dose1		•		•			•	
		•					•	
Dose3					D1		•	
Jones	heere				Dosel			
	L						*****	*****
PARAMETR Anal	RIC ANA ysis o merator	ALYSES of Varia	- use al nce (ANOVA Denominato	pha-level) - overa	l=0.05 for a all F-test F-stat			
	3		12		1.39	0.292		
MannWhit Jonckhee	: - tes ere - t	sting ea test ass	ch trt med umes dose-	ian sign: response	if. differer relationshi	nt from cor Lp, testing	ntrol J INCREASING to	rend
Level	Med	dian	Mann	Whit p-va	alue	Jonckhe	eere p-value	
Ctrl		,						
Dose1								
Dose2								
Dose3								
	heere				Dose1	L		
test for	fish	screen LTS FOR	study – Cy VARIABLE V	permethr: AR16 ()	in M 17b-estrac	diol (ng/mI	2))	
Shapiro- Levenes Use para	Wilks test f	test for homo analys	geneity of es if neit	y of Resi variance her test Levene Test S	iduals al e(absolute r rejected, c es Levene tat P-valu	residuals) otherwise r es Conclu re	alpha-level non-parametric usion	L=0.05 analyses
					•	NO DAT	TA FOR TEST	
******	*****	*****	*****	******	******	******	******	****
BASIC SU	MMARY	STATIST	ICS					

						EPA	MRID Numbe	48683001
Level	N	Mean	StdDev	StdEer	Coef of	Var	95% Conf In	terval
Ctrl	• •			Deall	0001 01	V () L		CCIVUI
Dosel	_	•	•	•	•		. ,	•
Dose2		•	•	•	•		. ,	•
Dose3		:		:			. ,	
Level		Median	Min	Max	%of Control	(means)	%Reducti	on(means)
Ctrl		rica Lan	111	1107	OUL CONCION	(means)	41/600CC	on (means)
Dosel		•	•	•	•			
Dose2		•	•	•	•		•	
Dose3		•	•	•	•			
Doses		-	•	•	•		•	
*****	****	*****			******	*****	* * * * * * * * * * * * * * * * * * * *	***
					0.05 for al	.i tests		
			ance (ANOVA					
Nu					stat			
		3	12	1	39	0.292		
					. different elationship			trend
Level	_	Median	Mann	Whit p-val	ue	Jonck	heere p-val	ue
Ctrl								
Dosel				•			•	
Dose2								
Dose3								
Jone	khee	re			Dose1			
****	****	*****	****	******	****	****	******	*****
			- use al ance (ANOV <i>A</i>		0.05 for al	l tests		
	_		Denominato	-		P-value		
144.		3	12		.39			
	t - 1	testing ea	ach trt med	lian signif	. different	from c		NG trend
COMORNIC		0000 000	2200 4050	Looponbe I		,		
Level	1	1edian	Mann	Whit p-val	ue	Jonck	heere p-val	ue
Ctrl		•						
Dosel							•	
Dose2								
Dose3								
Jone	kheer	re			Dosel			